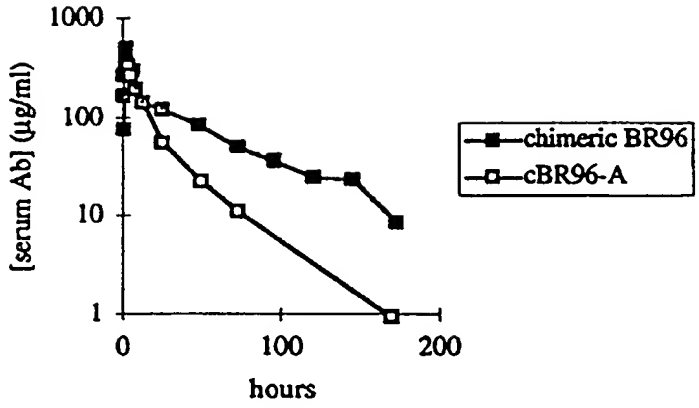
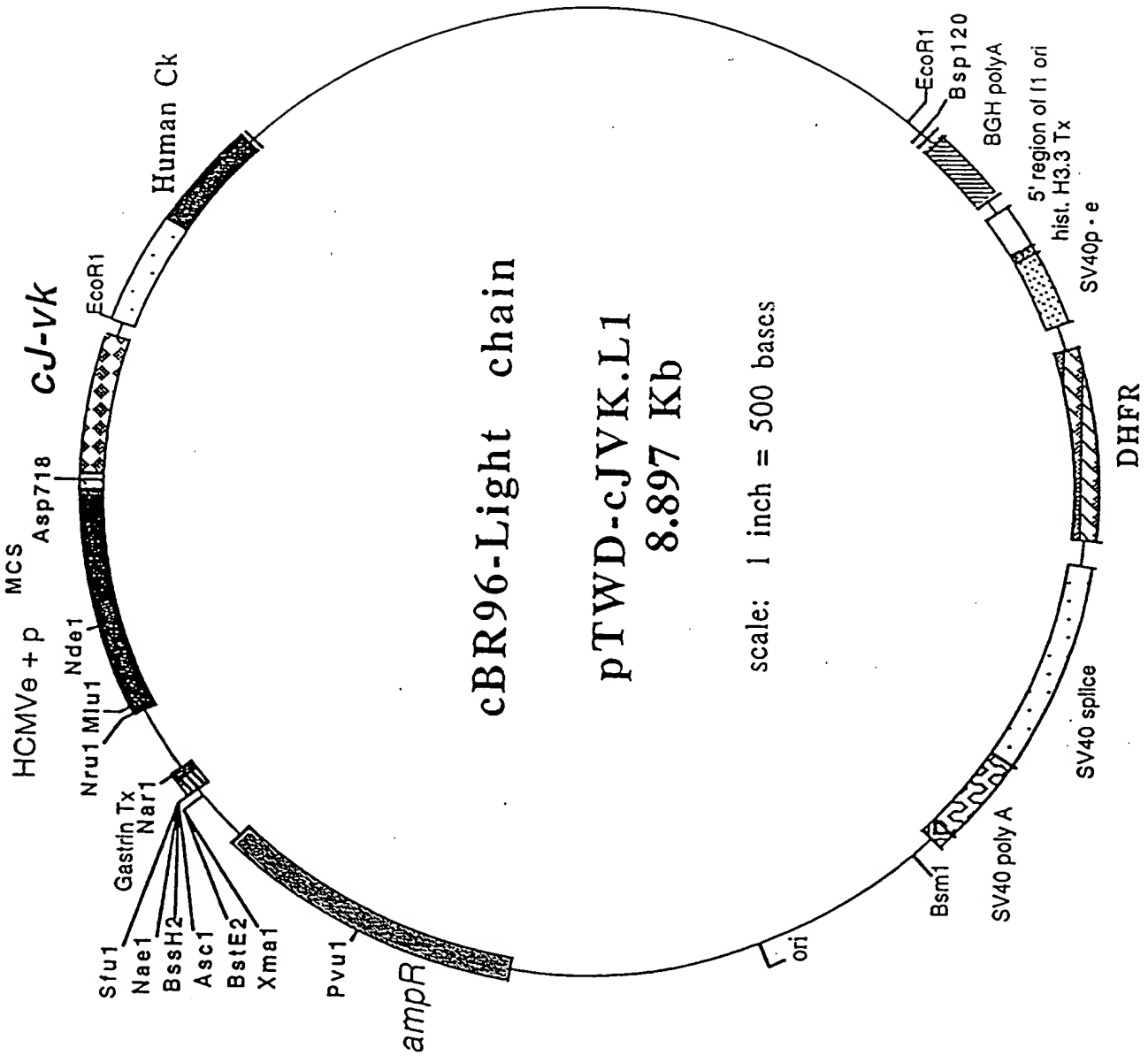


Figure 1. Plasma clearance in high LeY expressing dogs chimeric versus constant region mutant of cBR96-2.

Figure One

Figure 2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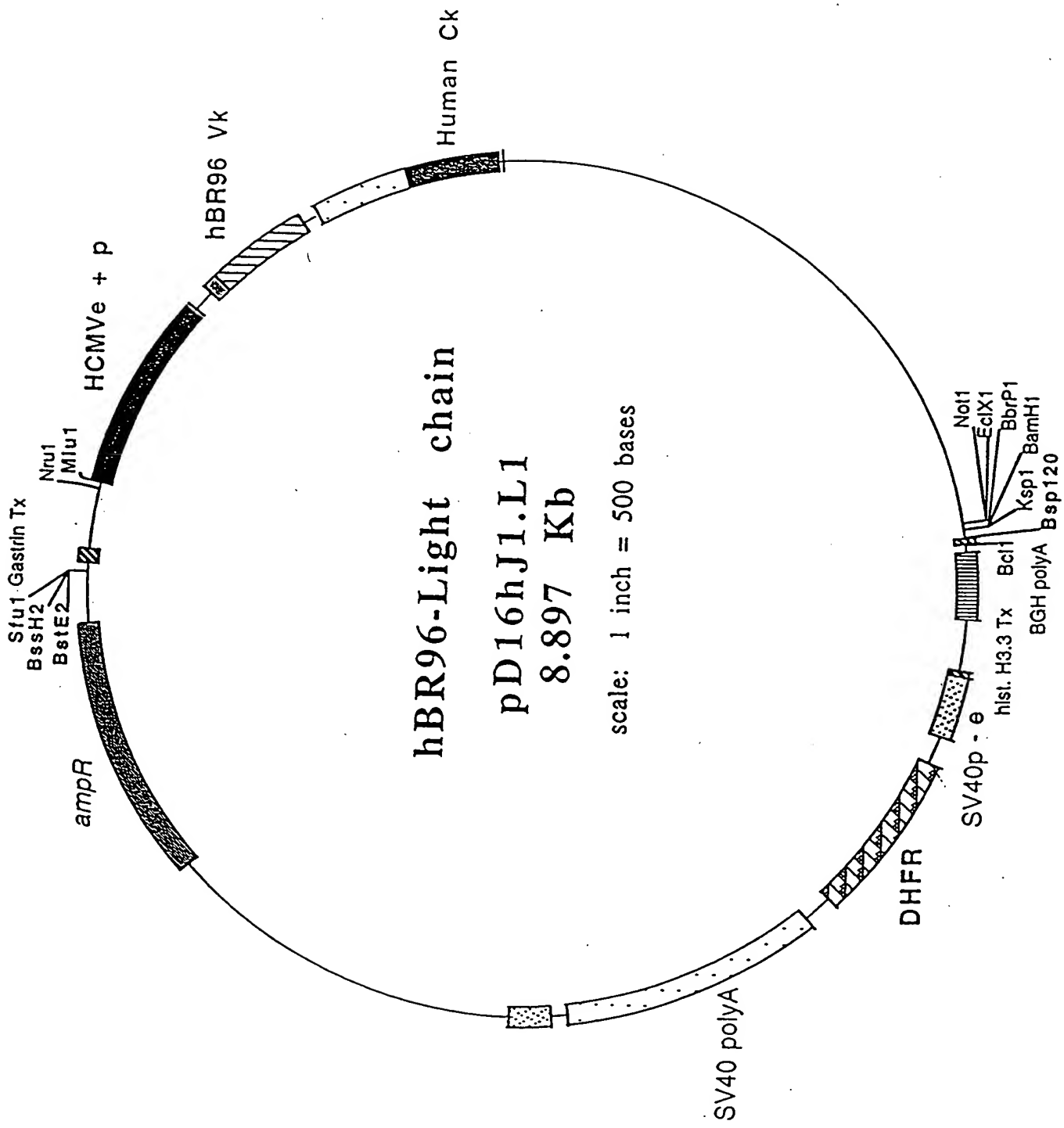
pTWD-cJVK.L1
8.897 Kb
scale: 1 inch = 500 bases
HCMVe + p
MCS
Asp718
cJ-vk
Human Ck
EcoR1
Nde1
Mlu1
Nru1
Nar1
Gastrin Tx
Sfu1
Nae1
BssH2
Asc1
BstE2
Xma1
Pvu1
ampR
ori
Bsm1
SV40 poly A
SV40 splice
DHFR
SV40p - e
5' region of I1 ori
hist. H3.3 Tx
BGH polyA
Bsp120
EcoR1

Figure 3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8.897 Kb
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Human Ck
hBR96 Vk
HCMVe + p
Nru1
Mlu1
Sfu1 GastrIn Tx
BssH2
BstE2
ampR
SV40 polyA
DHFR
SV40p - e
hist. H3.3 Tx
BclI
BGH polyA
Not1
EclX1
BbrP1
Ksp1
BamH1
Bsp120

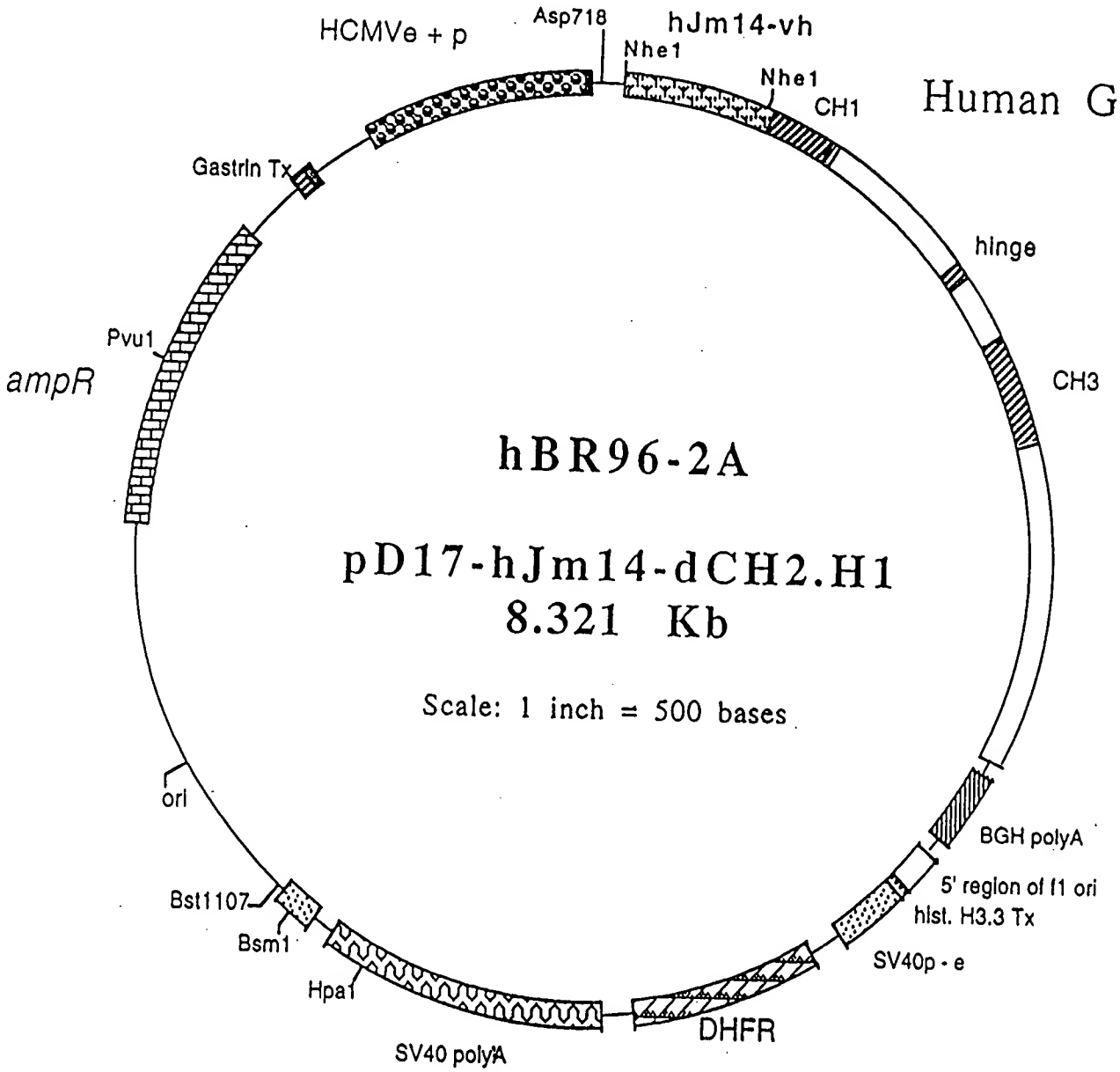
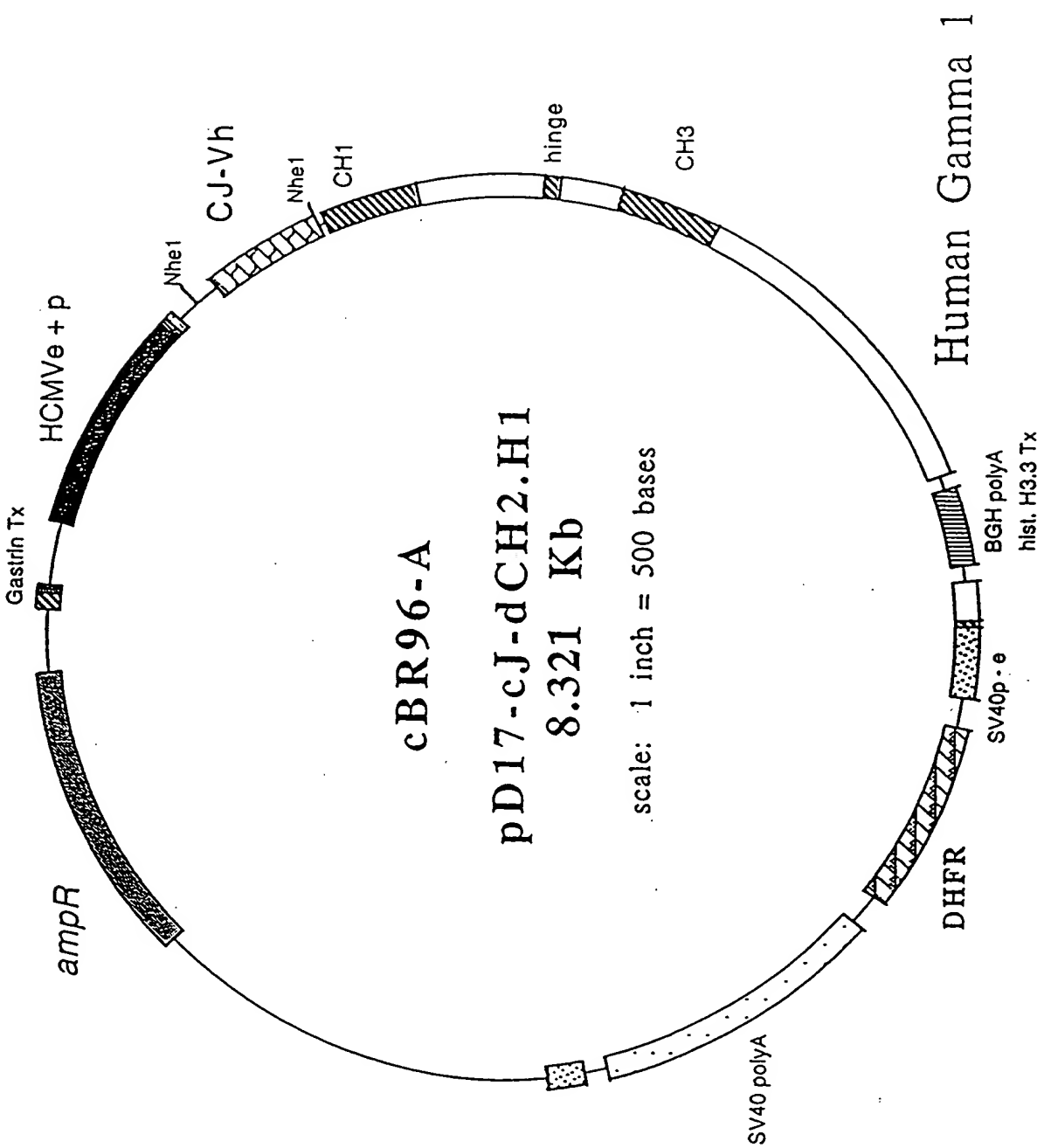


Figure 4

Figure 5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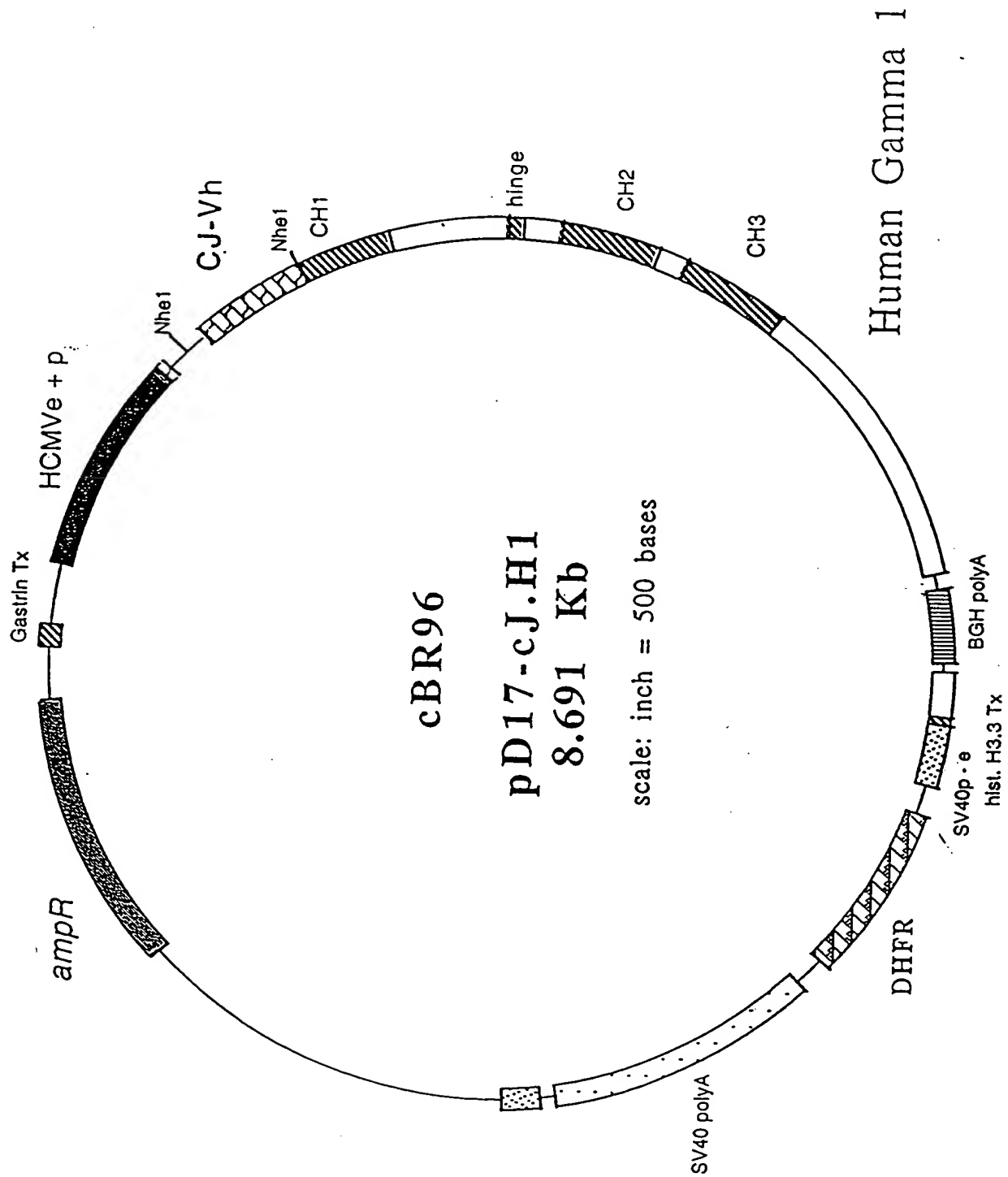
pD17-cJ-dCH2.H1
8.321 Kb
scale: 1 inch = 500 bases
ampR
Gastrin Tx
HCMVe + p
Nhe1
CJ-Vh
Nhe1
CH1
hinge
CH3
Human Gamma 1
BGH polyA
hist. H3.3 Tx
SV40p - e
DHFR
SV40 polyA

Figure 6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pD17-cJ.H1
8.691 Kb
scale: inch = 500 bases
Human Gamma 1
CJ-Vh
Nhe1
CH1
hinge
CH2
CH3
HCMVe + p
Gastrln Tx
ampR
SV40 polyA
DHFR
SV40p - e
hist. H3.3 Tx
BGH polyA

Figure 7

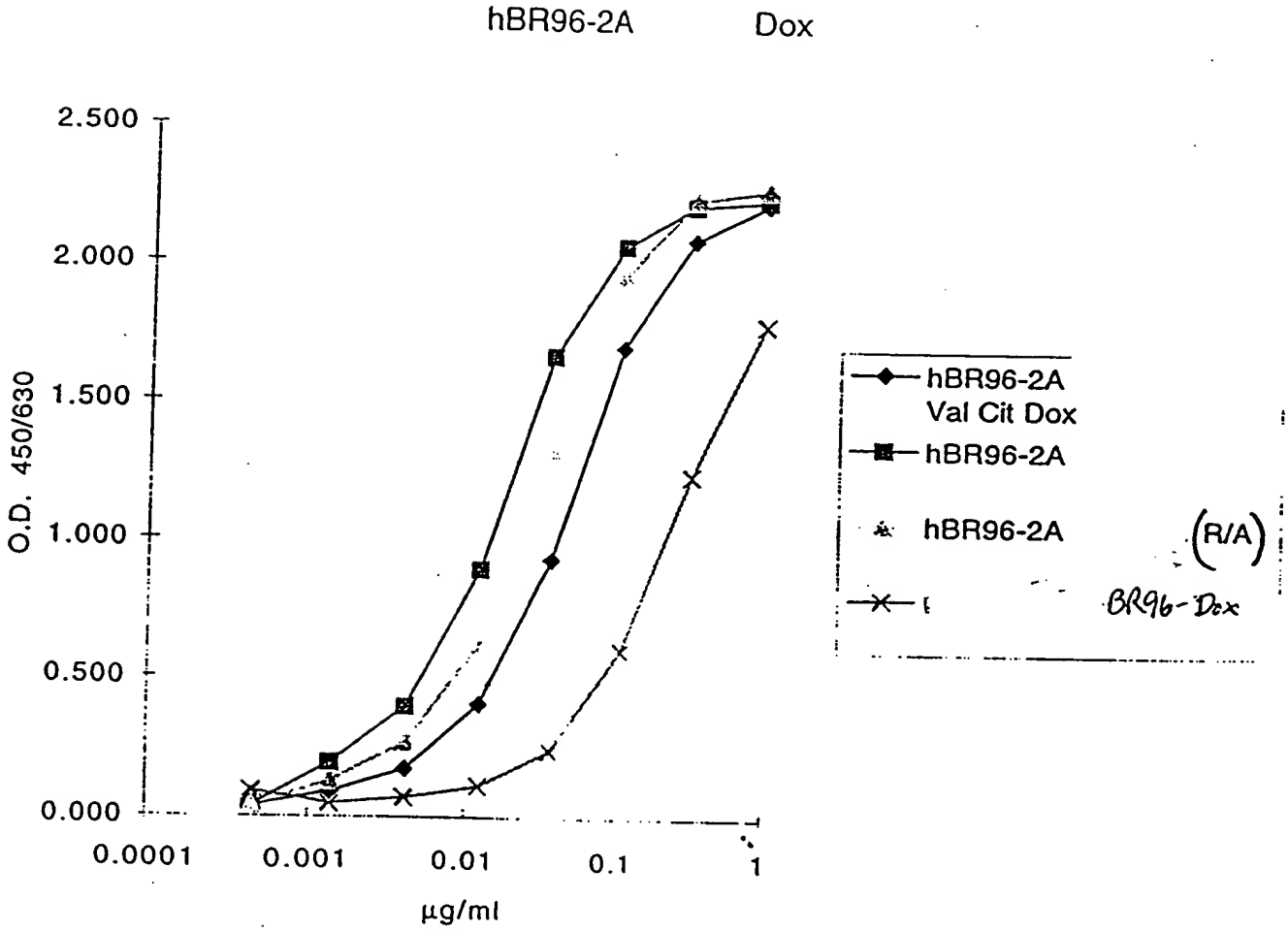
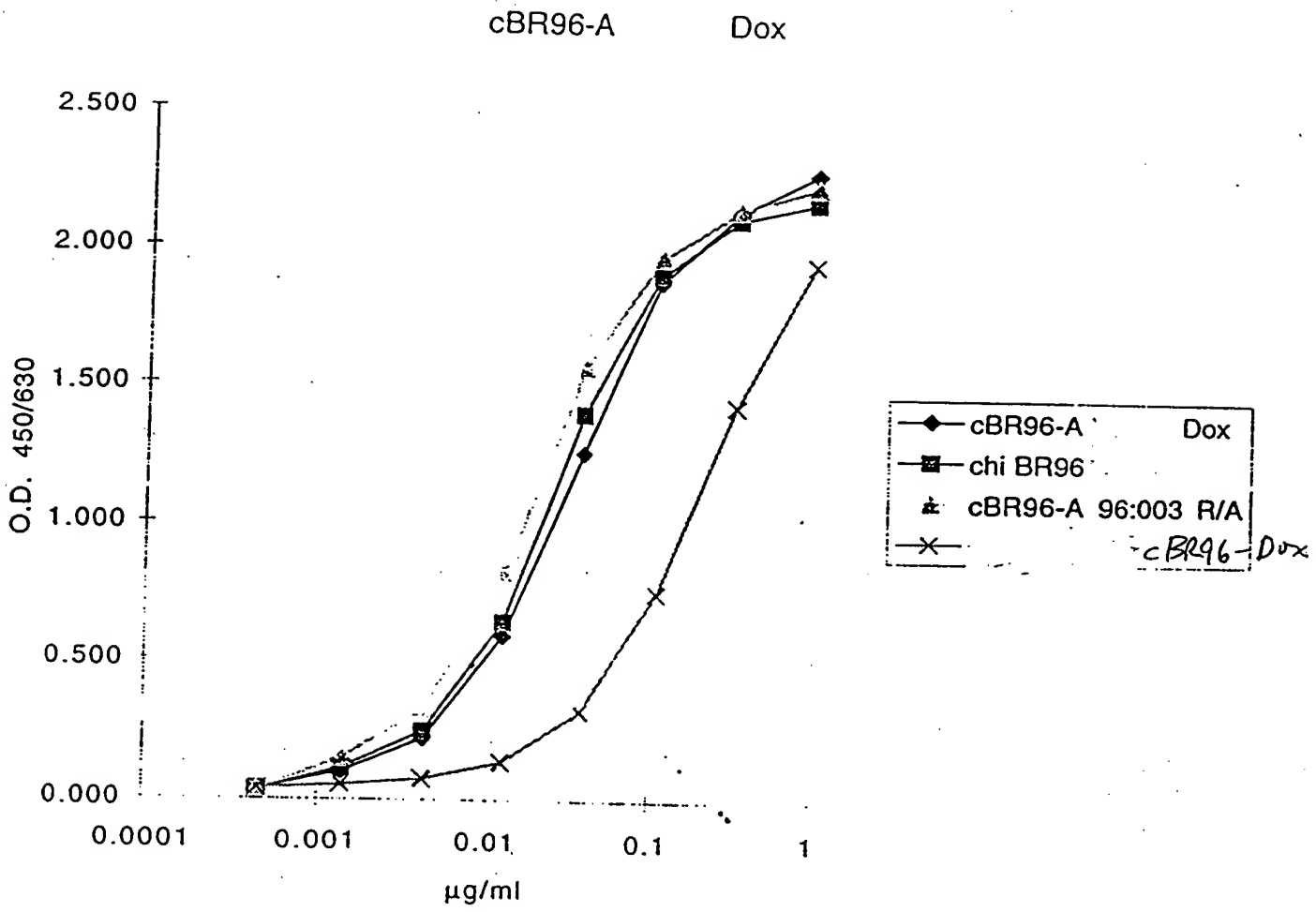
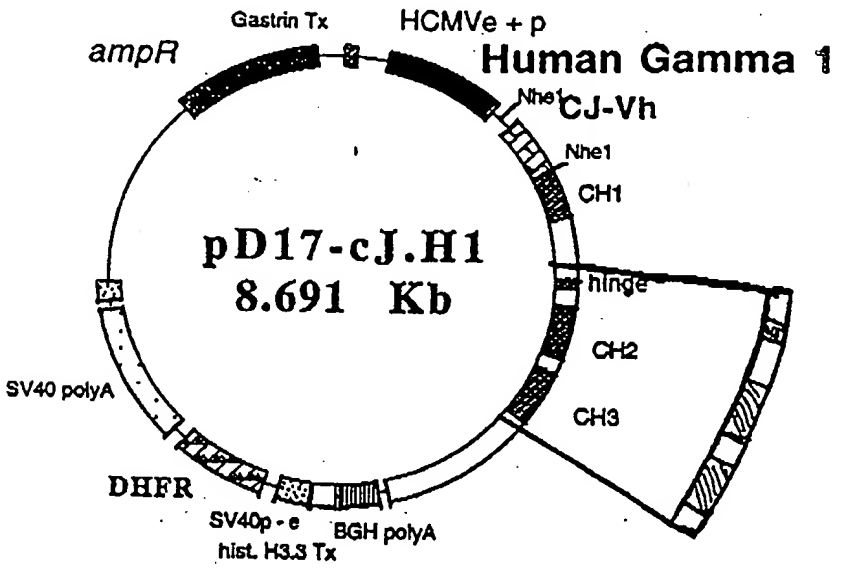

hBR96-2A
Dox
2.500
2.000
1.500
1.000
0.500
0.000
O.D. 450/630
0.0001
0.001
0.01
0.1
1
µg/ml
hBR96-2A
Val Cit Dox
hBR96-2A
hBR96-2A
(R/A)
BR96-Dox

Figure 8


cBR96-A
Dox
2.500
2.000
1.500
1.000
0.500
0.000
O.D. 450/630
0.0001
0.001
0.01
0.1
1
µg/ml
cBR96-A Dox
chi BR96
cBR96-A 96:003 R/A
cBR96-Dox

A- Hinge + CH2 + CH3 domains were removed from BR96 IgG1 construct by E. [redacted] III restriction digestion .



B. 1 - Hinge + CH3 domains amplified by PCR from L6 IgG1 construct lacking the CH2 domain .

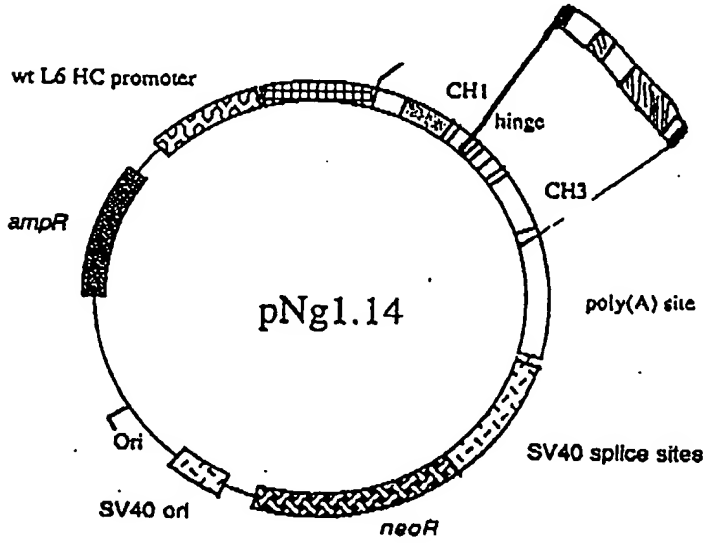


Figure 9

CH3 - Hinge +CH3 PCR fragment cloned by homologous recombination into E.co47-III site of BR96 IgG1 molecule.

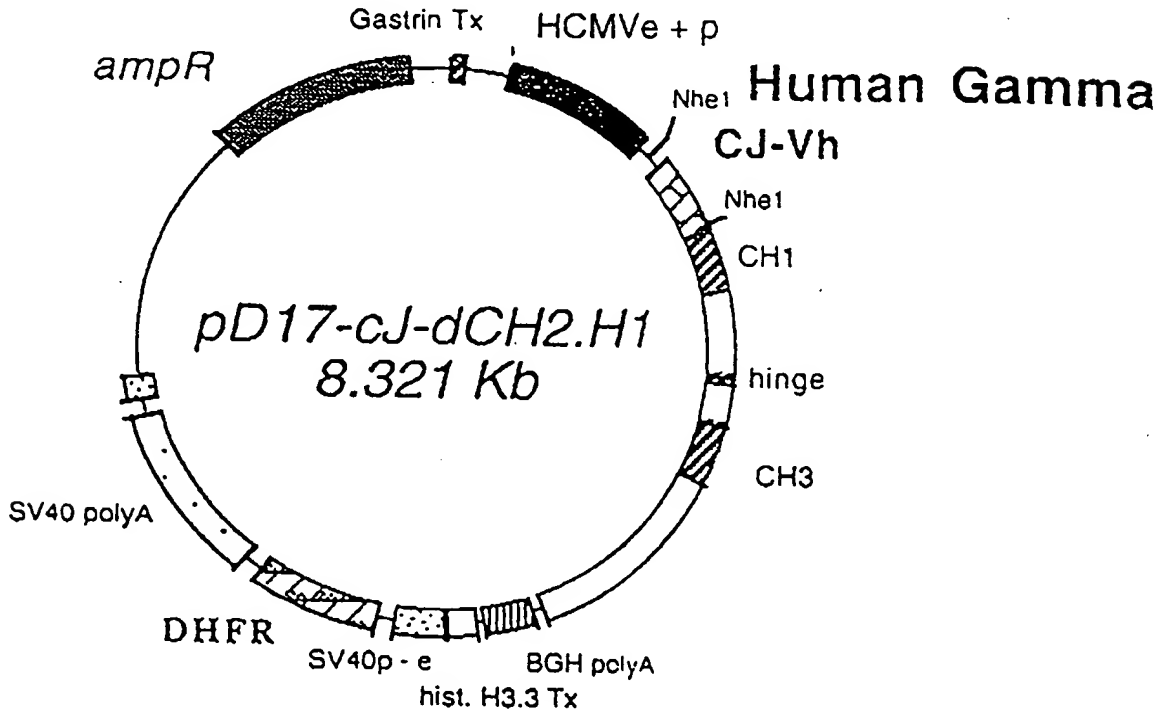
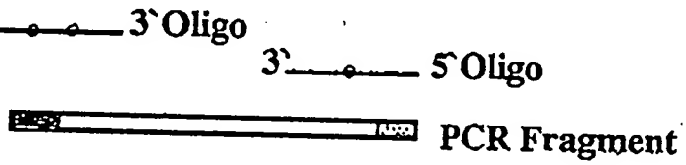


Figure 9

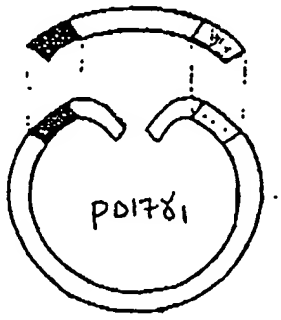
(CONTINUED)

1- Introduction of mutations by site-directed mutagenesis on double-stranded plasmid DNA.

A- Mutations introduced into synthetic oligonucleotides used for the PCR amplification of CH2 domain.



B- Plasmid DNA linearized inside CH2 domain and co-transformed with PCR fragment into competent DH5α.



C- Cloning mediated by homologous recombination yields transformants harbouring recombinant plasmids.

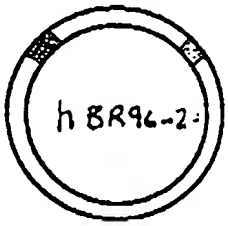
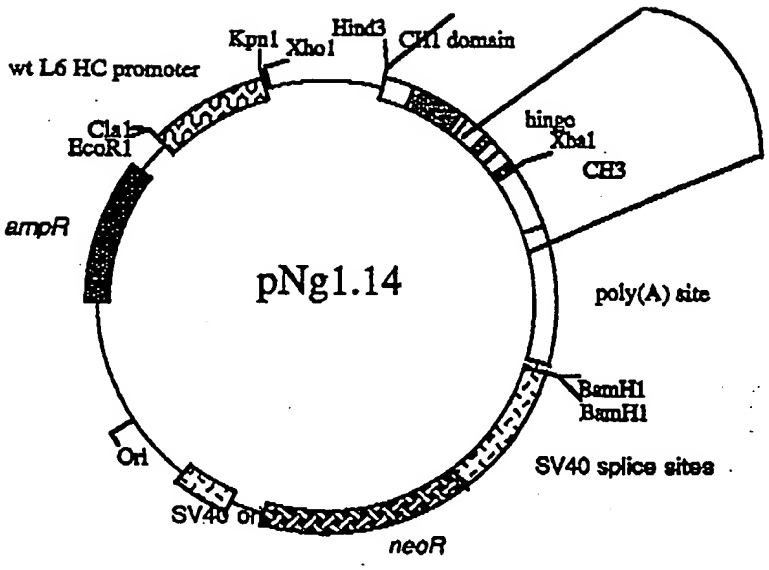


Figure 10

Figure 11


wt L6 HC promoter
Kpn1
Xho1
Hind3
CH1 domain
hinge
Xba1
CH3
Cla1
EcoR1
ampR
pNg1.14
poly(A) site
BamH1
BamH1
SV40 splice sites
Ori
SV40 ori
neoR

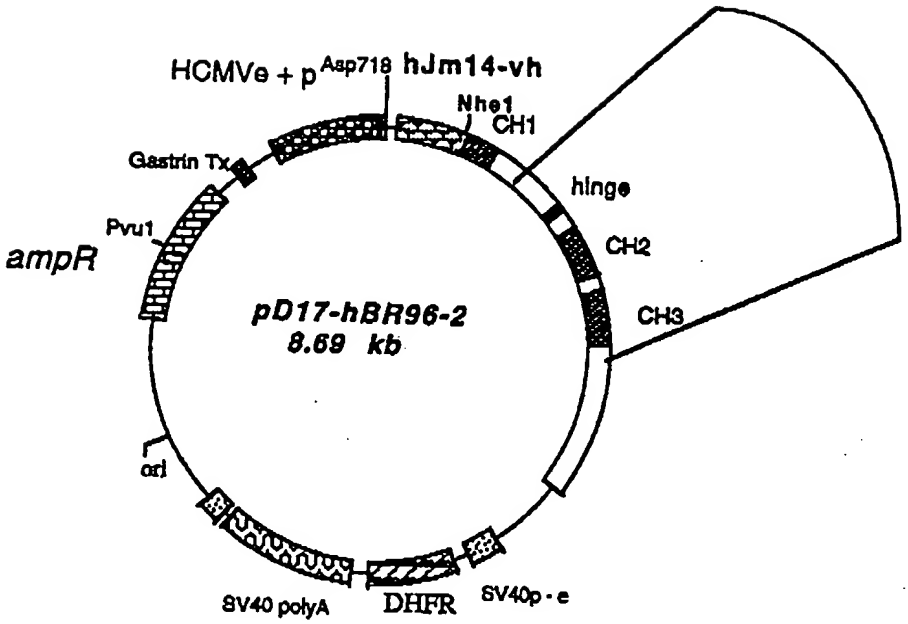


Figure 12

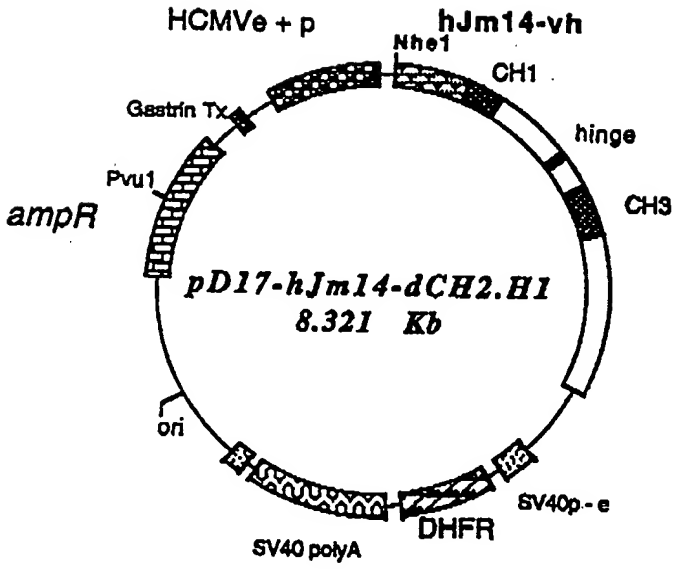


Figure 13

pD17-cJ-dCH2.H1

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CTGCCTAGCC CTCTAGACGA TCCACTGGAC TCCGCGCGGC CGAAGCTTAT CGGTCTCATT GGAAAAAAAA ATTAAAATAA AATAAAATAA

       100        110        120        130        140        150        160        170        180
TTTGAGATGG AGTTTGGCGC CGATCTCCCG ATCCCCTATG GTCGACTCTC AGTACAATCT GCTCTGATGC CGCATAGTTA AGCCAGTATC
AAACTCTACC TCAAACCGCG GCTAGAGGGC TAGGGGATAC CAGCTGAGAG TCATGTTAGA CGAGACTACG GCGTATCAAT TCGGTCATAG

       190        200        210        220        230        240        250        260        270
TGCTCCCTGC TTGTGTGTTG GAGGTCGCTG AGTAGTGCGC GAGCAAAATT TAAGCTACAA CAAGGCAAGG CTTGACCGAC AATTGCATGA
ACGAGGGACG AACACACAAC CTCCAGCGAC TCATCACGCG CTCGTTTTAA ATTCGATGTT GTTCCGTTCC GAACTGGCTG TTAACGTACT

       280        290        300        310        320        330        340        350        360
AGAATCTGCT TAGGGTTAGG CGTTTTGCGC TGCTTCGCGA TGTACGGGCC AGATATACGC GTTGACATTG ATTATTGACT AGTTATTAAT
TCTTAGACGA ATCCCAATCC GCAAAACGCG ACGAAGCGCT ACATGCCCGG TCTATATGCG CAACTGTAAC TAATAACTGA TCAATAATTA

       370        380        390        400        410        420        430        440        450
AGTAATCAAT TACGGGGTCA TTAGTTCATA GCCCATATAT GGAGTTCCGC GTTACATAAC TTACGGTAAA TGGCCCGCCT GGCTGACCGC
TCATTAGTTA ATGCCCCAGT AATCAAGTAT CGGGTATATA CCTCAAGGCG CAATGTATTG AATGCCATTT ACCGGGCGGA CCGACTGGCG

       460        470        480        490        500        510        520        530        540
CCAACGACCC CCGCCCATTG ACGTCAATAA TGACGTATGT TCCCATAGTA ACGCCAATAG GGACTTTCCA TTGACGTCAA TGGGTGGACT
GGTTGCTGGG GGCGGGTAAC TGCAGTTATT ACTGCATACA AGGGTATCAT TGCGGTTATC CCTGAAAGGT AACTGCAGTT ACCCACCTGA

       550        560        570        580        590        600        610        620        630
ATTTACGGTA AACTGCCCAC TTGGCAGTAC ATCAAGTGTA TCATATGCCA AGTACGCCCC CTATTGACGT CAATGACGGT AAATGGCCCG
TAAATGCCAT TTGACGGGTG AACCGTCATG TAGTTCACAT AGTATACGGT TCATGCGGGG GATAACTGCA GTTACTGCCA TTTACCGGGC

       640        650        660        670        680        690        700        710        720
CCTGGCATTA TGCCCAGTAC ATGACCTTAT GGGACTTTCC TACTTGGCAG TACATCTACG TATTAGTCAT CGCTATTACC ATGGTGATGC
GGACCGTAAT ACGGGTCATG TACTGGAATA CCCTGAAAGG ATGAACCGTC ATGTAGATGC ATAATCAGTA GCGATAATGG TACCACTACG

       730        740        750        760        770        780        790        800        810
GGTTTTGGCA GTACATCAAT GGGCGTGGAT AGCGGTTTGA CTCACGGGGA TTTCCAAGTC TCCACCCCAT TGACGTCAAT GGGAGTTTGT
CCAAAACCGT CATGTAGTTA CCCGCACCTA TCGCCAAACT GAGTGCCCCT AAAGGTTCAG AGGTGGGGTA ACTGCAGTTA CCCTCAAACA

       820        830        840        850        860        870        880        890        900
TTTGGCACCA AAATCAACGG GACTTTCCAA AATGTCGTAA CAACTCCGCC CCATTGACGC AAATGGGCGG TAGGCGTGTA CGGTGGGAGG
AAACCGTGGT TTTAGTTGCC CTGAAAGGTT TTACAGCATT GTTGAGGCGG GGTAACTGCG TTTACCCGCC ATCCGCACAT GCCACCCTCC
```

Figure 14

pD17-cJ-dCH2.H1

```
       910        920        930        940        950        960        970        980        990
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AGATATATTC GTCTCGAGAG ACCGATTGAT CTCTTGGGTG ACGAATGACC GAATAGCTTT AATTATGCTG AGTGATATCC CTCTGGGTTC

      1000       1010       1020       1030       1040       1050       1060       1070       1080
CTTGGTACCA ATTTAAATTG ATATCTCCTT AGGTCTCGAG TCTCTAGATA ACCGGTCAAT CGATTGGAAT TCTTGCGGCC GCTTGCTAGC
GAACCATGGT TAAATTTAAC TATAGAGGAA TCCAGAGCTC AGAGATCTAT TGGCCAGTTA GCTAACCTTA AGAACGCCGG CGAACGATCG

      1090       1100       1110       1120       1130       1140       1150       1160       1170
CACCATGGAG TTGTGGTTAA GCTTGGTCCT TCCTTGTCCT TGTTTTAAAA GGTGTCCAGT GTGAAGTGAA TCTGGTGGAG TCTGGGGGAG
GTGGTACCTC AACACCAATT CGAACCAGGA AGGAACAGGA ACAAAATTTT CCACAGGTCA CACTTCACTT AGACCACCTC AGACCCCCTC

      1180       1190       1200       1210       1220       1230       1240       1250       1260
GCTTAGTGCA GCCTGGAGGG TCCCTGAAAG TCTCCTGTGT AACCTCTGGA TTCACTTTCA GTGACTATTA CATGTATTGG GTTCGCCAGA
CGAATCACGT CGGACCTCCC AGGGACTTTC AGAGGACACA TTGGAGACCT AAGTGAAAGT CACTGATAAT GTACATAACC CAAGCGGTCT

      1270       1280       1290       1300       1310       1320       1330       1340       1350
CTCCAGAGAA GAGGCTGGAG TGGGTCGCAT ACATTAGTCA AGGTGGTGAT ATAACCGACT ATCCAGACAC TGTAAAGGGT CGATTCACCA
GAGGTCTCTT CTCCGACCTC ACCCAGCGTA TGTAATCAGT TCCACCACTA TATTGGCTGA TAGGTCTGTG ACATTTCCCA GCTAAGTGGT

      1360       1370       1380       1390       1400       1410       1420       1430       1440
TCTCCAGAGA CAATGCCAAG AACACCCTGT ACCTGCAAAT GAGCCGTCTG AAGTCTGAGG ACACAGCCAT GTATTACTGT GCAAGAGGCC
AGAGGTCTCT GTTACGGTTC TTGTGGGACA TGGACGTTTA CTCGGCAGAC TTCAGACTCC TGTGTCGGTA CATAATGACA CGTTCTCCGG

      1450       1460       1470       1480       1490       1500       1510       1520       1530
TGGACGACGG GGCCTGGTTT GCTTACTGGG GCCAAGGGAC TCTGGTCACG GTCTCTGTAG CTAGCACCAA GGGCCCATCG GTCTTCCCCC
ACCTGCTGCC CCGGACCAAA CGAATGACCC CGGTTCCCTG AGACCAGTGC CAGAGACATC GATCGTGGTT CCCGGGTAGC CAGAAGGGGG

      1540       1550       1560       1570       1580       1590       1600       1610       1620
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ACCGTGGGAG GAGGTTCTCG TGGAGACCCC CGTGTCGCCG GGACCCGACG GACCAGTTCC TGATGAAGGG GCTTGGCCAC TGCCACAGCA

      1630       1640       1650       1660       1670       1680       1690       1700       1710
GGAACTCAGG CGCCCTGACC AGCGGCGTGC ACACCTTCCC GGCTGTCCTA CAGTCCTCAG GACTCTACTC CCTCAGCAGC GTGGTCACCG
CCTTGAGTCC GCGGGACTGG TCGCCGCACG TGTGGAAGGG CCGACAGGAT GTCAGGAGTC CTGAGATGAG GGAGTCGTCG CACCAGTGGC

      1720       1730       1740       1750       1760       1770       1780       1790       1800
TGCCCTCCAG CAGCTTGGGC ACCCAGACCT ACATCTGCAA CGTGAATCAC AAGCCCAGCA ACACCAAGGT GGACAAGAAA GTTGGTGAGA
ACGGGAGGTC GTCGAACCCG TGGGTCTGGA TGTAGACGTT GCACTTAGTG TTCGGGTCGT TGTGGTTCCA CCTGTTCTTT CAACCACTCT
```

Figure 14
(continued)

pD17-cJ-dCH2.H1

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GGCCAGCACA GGGAGGGAGG GTGTCTGCTG GAAGCCAGGC TCAGCGCTCC TGCCTGGACG CATCCCGGCT ATGCAGCCCC AGTCCAGGGC
CCGGTCGTGT CCCTCCCTCC CACAGACGAC CTTCGGTCCG AGTCGCGAGG ACGGACCTGC GTAGGGCCGA TACGTCGGGG TCAGGTCCCG

      1900        1910        1920        1930        1940        1950        1960        1970        1980
AGCAAGGCAG GCCCCGTCTG CCTCTTCACC CGGAGGCCTC TGCCCGCCCC ACTCATGCTC AGGGAGAGGG TCTTCTGGCT TTTTCCCCAG
TCGTTCCGTC CGGGGCAGAC GGAGAAGTGG GCCTCCGGAG ACGGGCGGGG TGAGTACGAG TCCCTCTCCC AGAAGACCGA AAAAGGGGTC

      1990        2000        2010        2020        2030        2040        2050        2060        2070
GCTCTGGGCA GGCACAGGCT AGGTGCCCCT AACCCAGGCC CTGCACACAA AGGGGCAGGT GCTGGGCTCA GACCTGCCAA GAGCCATATC
CGAGACCCGT CCGTGTCCGA TCCACGGGGA TTGGGTCCGG GACGTGTGTT TCCCCGTCCA CGACCCGAGT CTGGACGGTT CTCGGTATAG

      2080        2090        2100        2110        2120        2130        2140        2150        2160
CGGGAGGACC CTGCCCCTGA CCTAAGCCCA CCCCAAAGGC CAAACTCTCC ACTCCCTCAG CTCGGACACC TTCTCTCCTC CCAGATTCCA
GCCCTCCTGG GACGGGGACT GGATTCGGGT GGGGTTTCCG GTTTGAGAGG TGAGGGAGTC GAGCCTGTGG AAGAGAGGAG GGTCTAAGGT

      2170        2180        2190        2200        2210        2220        2230        2240        2250
GTAACTCCCA ATCTTCTCTC TGCAGAGCCC AAATCTTGTG ACAAAACTCA CACATGCCCA CCGTGCCCAG GTAAGCCAGC CCAGGCCTCG
CATTGAGGGT TAGAAGAGAG ACGTCTCGGG TTTAGAACAC TGTTTTGAGT GTGTACGGGT GGCACGGGTC CATTCGGTCG GGTCCGGAGC

      2260        2270        2280        2290        2300        2310        2320        2330        2340
CCCTCCAGCT CAAGGCGGGA CAGGTGCCCT AGAGTAGCCT GCATCCAGGG ACACACCACG TGGGTACCAA CATGTCCGGA GCCACATGGA
GGGAGGTCGA GTTCCGCCCT GTCCACGGGA TCTCATCGGA CGTAGGTCCC TGTGTGGTGC ACCCATGGTT GTACAGGCCT CGGTGTACCT

      2350        2360        2370        2380        2390        2400        2410        2420        2430
CAGAGGCCGG CTCGGCCCAC CCTCTGCCCT GAGAGTGACC GCTGTACCAA CCTCTGTCCC TACAGGGCAG CCCCGAGAAC CACAGGTGTA
GTCTCCGGCC GAGCCGGGTG GGAGACGGGA CTCTCACTGG CGACATGGTT GGAGACAGGG ATGTCCCGTC GGGGCTCTTG GTGTCCACAT

      2440        2450        2460        2470        2480        2490        2500        2510        2520
CACCCTGCCC CCATCCCGGG ATGAGCTGAC CAAGAACCAG GTCAGCCTGA CCTGCCTGGT CAAAGGCTTC TATCCCAGCG ACATCGCCGT
GTGGGACGGG GGTAGGGCCC TACTCGACTG GTTCTTGGTC CAGTCGGACT GGACGGACCA GTTTCCGAAG ATAGGGTCGC TGTAGCGGCA

      2530        2540        2550        2560        2570        2580        2590        2600        2610
GGAGTGGGAG AGCAATGGGC AGCCGGAGAA CAACTACAAG ACCACGCCTC CCGTGCTGGA CTCCGACGGC TCCTTCTTCC TCTACAGCAA
CCTCACCCTC TCGTTACCCG TCGGCCTCTT GTTGATGTTC TGGTGCGGAG GGCACGACCT GAGGCTGCCG AGGAAGAAGG AGATGTCGTT

      2620        2630        2640        2650        2660        2670        2680        2690        2700
GCTCACCGTG GACAAGAGCA GGTGGCAGCA GGGGAACGTC TTCTCATGCT CCGTGATGCA TGAGGCTCTG CACAACCACT ACACGCAGAA
CGAGTGGCAC CTGTTCTCGT CCACCGTCGT CCCCTTGCAG AAGAGTACGA GGCACTACGT ACTCCGAGAC GTGTTGGTGA TGTGCGTCTT
```

Figure 14
(continued)

pD17-cJ-dCH2.H1

```
      2710        2720        2730        2740        2750        2760        2770        2780        2790
GAGCCTCTCC CTGTCTCCGG GTAAATGAGT GCGACGGCCG GCAAGCCCCC GCTCCCCGGG CTCTCGCGGT CGCACGAGGA TGCTTGGCAC
CTCGGAGAGG GACAGAGGCC CATTTACTCA CGCTGCCGGC CGTTCGGGGG CGAGGGGCCC GAGAGCGCCA GCGTGCTCCT ACGAACCGTG

      2800        2810        2820        2830        2840        2850        2860        2870        2880
GTACCCCCTG TACATACTTC CCGGGCGCCC AGCATGGAAA TAAAGCACCC AGCGCTGCCC TGGGCCCCTG CGAGACTGTG ATGGTTCTTT
CATGGGGGAC ATGTATGAAG GGCCCGCGGG TCGTACCTTT ATTTCGTGGG TCGCGACGGG ACCCGGGGAC GCTCTGACAC TACCAAGAAA

      2890        2900        2910        2920        2930        2940        2950        2960        2970
CCACGGGTCA GGCCGAGTCT GAGGCCTGAG TGGCATGAGG GAGGCAGAGC GGGTCCCACT GTCCCCACAC TGGCCCAGGC TGTGCAGGTG
GGTGCCCAGT CCGGCTCAGA CTCCGGACTC ACCGTACTCC CTCCGTCTCG CCCAGGGTGA CAGGGGTGTG ACCGGGTCCG ACACGTCCAC

      2980        2990        3000        3010        3020        3030        3040        3050        3060
TGCCTGGGCC CCCTAGGGTG GGGCTCAGCC AGGGGCTGCC CTCGGCAGGG TGGGGGATTT GCCAGCGTGG CCCTCCCTCC AGCAGCACCT
ACGGACCCGG GGGATCCCAC CCCGAGTCGG TCCCCGACGG GAGCCGTCCC ACCCCCTAAA CGGTCGCACC GGGAGGGAGG TCGTCGTGGA

      3070        3080        3090        3100        3110        3120        3130        3140        3150
GCCCTGGGCT GGGCCACGGG AAGCCCTAGG AGCCCCTGGG GACAGACACA CAGCCCCTGC CTCTGTAGGA GACTGTCCTG TTCTGTGAGC
CGGGACCCGA CCCGGTGCCC TTCGGGATCC TCGGGGACCC CTGTCTGTGT GTCGGGGACG GAGACATCCT CTGACAGGAC AAGACACTCG

      3160        3170        3180        3190        3200        3210        3220        3230        3240
GCCCCTGTCC TCCCGACCTC CATGCCCACT CGGGGGCATG CCTAGTCCAT GTGCGTAGGG ACAGGCCCTC CCTCACCCAT CTACCCCCAC
CGGGGACAGG AGGGCTGGAG GTACGGGTGA GCCCCCGTAC GGATCAGGTA CACGCATCCC TGTCCGGGAG GGAGTGGGTA GATGGGGGTG

      3250        3260        3270        3280        3290        3300        3310        3320        3330
GGCACTAACC CCTGGCTGCC CTGCCCAGCC TCGCACCCGC ATGGGGACAC AACCGACTCC GGGGACATGC ACTCTCGGGC CCTGTGGAGG
CCGTGATTGG GGACCGACGG GACGGGTCGG AGCGTGGGCG TACCCCTGTG TTGGCTGAGG CCCCTGTACG TGAGAGCCCG GGACACCTCC

      3340        3350        3360        3370        3380        3390        3400        3410        3420
GACTGGTGCA GATGCCCACA CACACACTCA GCCCAGACCC GTTCAACAAA CCCCGCACTG AGGTTGGCCG GCCACACGGC CACCACACAC
CTGACCACGT CTACGGGTGT GTGTGTGAGT CGGGTCTGGG CAAGTTGTTT GGGGCGTGAC TCCAACCGGC CGGTGTGCCG GTGGTGTGTG

      3430        3440        3450        3460        3470        3480        3490        3500        3510
ACACGTGCAC GCCTCACACA CGGAGCCTCA CCCGGGCGAA CTGCACAGCA CCCAGACCAG AGCAAGGTCC TCGCACACGT GAACACTCCT
TGTGCACGTG CGGAGTGTGT GCCTCGGAGT GGGCCCGCTT GACGTGTCGT GGGTCTGGTC TCGTTCCAGG AGCGTGTGCA CTTGTGAGGA

      3520        3530        3540        3550        3560        3570        3580        3590        3600
CGGACACAGG CCCCCACGAG CCCCACGCGG CACCTCAAGG CCCACGAGCC TCTCGGCAGC TTCTCCACAT GCTGACCTGC TCAGACAAAC
GCCTGTGTCC GGGGGTGCTC GGGGTGCGCC GTGGAGTTCC GGGTGCTCGG AGAGCCGTCG AAGAGGTGTA CGACTGGACG AGTCTGTTTG
```

Figure 14
(continued)

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      3610        3620        3630        3640        3650        3660        3670        3680        3690
CCAGCCCTCC TCTCACAAGG GTGCCCCTGC AGCCGCCACA CACACACAGG GGATCACACA CCACGTCACG TCCCTGGCCC TGGCCCACTT
GGTCGGGAGG AGAGTGTTCC CACGGGGACG TCGGCGGTGT GTGTGTGTCC CCTAGTGTGT GGTGCAGTGC AGGGACCGGG ACCGGGTGAA

      3700        3710        3720        3730        3740        3750        3760        3770        3780
CCCAGTGCCG CCCTTCCCTG CAGGACGGAT CAGCCTCGAC TGTGCCTTCT AGTTGCCAGC CATCTGTTGT TTGCCCCTCC CCCGTGCCTT
GGGTCACGGC GGGAAGGGAC GTCCTGCCTA GTCGGAGCTG ACACGGAAGA TCAACGGTCG GTAGACAACA AACGGGGAGG GGGCACGGAA

      3790        3800        3810        3820        3830        3840        3850        3860        3870
CCTTGACCCT GGAAGGTGCC ACTCCCACTG TCCTTTCCTA ATAAAATGAG GAAATTGCAT CGCATTGTCT GAGTAGGTGT CATTCTATTC
GGAACTGGGA CCTTCCACGG TGAGGGTGAC AGGAAAGGAT TATTTTACTC CTTTAACGTA GCGTAACAGA CTCATCCACA GTAAGATAAG

      3880        3890        3900        3910        3920        3930        3940        3950        3960
TGGGGGGTGG GGTGGGGCAG GACAGCAAGG GGGAGGATTG GGAAGACAAT AGCAGGCATG CTGGGGATGC GGTGGGCTCT ATGGCTTCTG
ACCCCCCACC CCACCCCGTC CTGTCGTTCC CCCTCCTAAC CCTTCTGTTA TCGTCCGTAC GACCCCTACG CCACCCGAGA TACCGAAGAC

      3970        3980        3990        4000        4010        4020        4030        4040        4050
AGGCGGAAAG AACCAGCTGG GGCTCTAGGG GGTATCCCCA CGCGCCCTGT AGCGGCGCAT TAAGCGCGGC GGGTGTGGTG GTTACGCGCA
TCCGCCTTTC TTGGTCGACC CCGAGATCCC CCATAGGGGT GCGCGGGACA TCGCCGCGTA ATTCGCGCCG CCCACACCAC CAATGCGCGT

      4060        4070        4080        4090        4100        4110        4120        4130        4140
GCGTGACCGC TACACTTGCC AGCGCCCTAG CGCCCGCTCC TTTCGCTTTC TTCCCTTCCT TTCTCGCCAC GTTCGCCGGG CCTCTCAAAA
CGCACTGGCG ATGTGAACGG TCGCGGGATC GCGGGCGAGG AAAGCGAAAG AAGGGAAGGA AAGAGCGGTG CAAGCGGCCC GGAGAGTTTT

      4150        4160        4170        4180        4190        4200        4210        4220        4230
AAGGGAAAAA AAGCATGCAT CTCAATTAGT CAGCAACCAT AGTCCCGCCC CTAACTCCGC CCATCCCGCC CCTAACTCCG CCCAGTTCCG
TTCCCTTTTT TTCGTACGTA GAGTTAATCA GTCGTTGGTA TCAGGGCGGG GATTGAGGCG GGTAGGGCGG GGATTGAGGC GGGTCAAGGC

      4240        4250        4260        4270        4280        4290        4300        4310        4320
CCCATTCTCC GCCCCATGGC TGACTAATTT TTTTTATTTA TGCAGAGGCC GAGGCCGCCT CGGCCTCTGA GCTATTCCAG AAGTAGTGAG
GGGTAAGAGG CGGGGTACCG ACTGATTAAA AAAAATAAAT ACGTCTCCGG CTCCGGCGGA GCCGGAGACT CGATAAGGTC TTCATCACTC

      4330        4340        4350        4360        4370        4380        4390        4400        4410
GAGGCTTTTT TGGAGGCCTA GGCTTTTGCA AAAAGCTTGG ACAGCTCAGG GCTGCGATTT CGCGCCAAAC TTGACGGCAA TCCTAGCGTG
CTCCGAAAAA ACCTCCGGAT CCGAAAACGT TTTTCGAACC TGTCGAGTCC CGACGCTAAA GCGCGGTTTG AACTGCCGTT AGGATCGCAC

      4420        4430        4440        4450        4460        4470        4480        4490        4500
AAGGCTGGTA GGATTTTATC CCCGCTGCCA TCATGGTTCG ACCATTGAAC TGCATCGTCG CCGTGTCCCA AAATATGGGG ATTGGCAAGA
TTCCGACCAT CCTAAAATAG GGGCGACGGT AGTACCAAGC TGGTAACTTG ACGTAGCAGC GGCACAGGGT TTTATACCCC TAACCGTTCT
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Figure 14
(continued)

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      4510        4520        4530        4540        4550        4560        4570        4580        4590
ACGGAGACCT ACCCTGGCCT CCGCTCAGGA ACGAGTTCAA GTACTTCCAA AGAATGACCA CAACCTCTTC AGTGGAAGGT AAACAGAATC
TGCCTCTGGA TGGGACCGGA GGCGAGTCCT TGCTCAAGTT CATGAAGGTT TCTTACTGGT GTTGGAGAAG TCACCTTCCA TTTGTCTTAG

      4600        4610        4620        4630        4640        4650        4660        4670        4680
TGGTGATTAT GGGTAGGAAA ACCTGGTTCT CCATTCCTGA GAAGAATCGA CCTTTAAAGG ACAGAATTAA TATAGTTCTC AGTAGAGAAC
ACCACTAATA CCCATCCTTT TGGACCAAGA GGTAAGGACT CTTCTTAGCT GGAAATTTCC TGTCTTAATT ATATCAAGAG TCATCTCTTG

      4690        4700        4710        4720        4730        4740        4750        4760        4770
TCAAAGAACC ACCACGAGGA GCTCATTTTC TTGCCAAAAG TTTGGATGAT GCCTTAAGAC TTATTGAACA ACCGGAATTG GCAAGTAAAG
AGTTTCTTGG TGGTGCTCCT CGAGTAAAAG AACGGTTTTC AAACCTACTA CGGAATTCTG AATAACTTGT TGGCCTTAAC CGTTCATTTC

      4780        4790        4800        4810        4820        4830        4840        4850        4860
TAGACATGGT TTGGATAGTC GGAGGCAGTT CTGTTTACCA GGAAGCCATG AATCAACCAG GCCACCTTAG ACTCTTTGTG ACAAGGATCA
ATCTGTACCA AACCTATCAG CCTCCGTCAA GACAAATGGT CCTTCGGTAC TTAGTTGGTC CGGTGGAATC TGAGAAACAC TGTTCCTAGT

      4870        4880        4890        4900        4910        4920        4930        4940        4950
TGCAGGAATT TGAAAGTGAC ACGTTTTTCC CAGAAATTGA TTTGGGGAAA TATAAACTTC TCCCAGAATA CCCAGGCGTC CTCTCTGAGG
ACGTCCTTAA ACTTTCACTG TGCAAAAAGG GTCTTTAACT AAACCCCTTT ATATTTGAAG AGGGTCTTAT GGGTCCGCAG GAGAGACTCC

      4960        4970        4980        4990        5000        5010        5020        5030        5040
TCCAGGAGGA AAAAGGCATC AAGTATAAGT TTGAAGTCTA CGAGAAGAAA GACTAACAGG AAGATGCTTT CAAGTTCTCT GCTCCCCTCC
AGGTCCTCCT TTTTCCGTAG TTCATATTCA AACTTCAGAT GCTCTTCTTT CTGATTGTCC TTCTACGAAA GTTCAAGAGA CGAGGGGAGG

      5050        5060        5070        5080        5090        5100        5110        5120        5130
TAAAGCTATG CATTTTTATA AGACCATGGG ACTTTTGCTG GCTTTAGATC TCTTTGTGAA GGAACCTTAC TTCTGTGGTG TGACATAATT
ATTTCGATAC GTAAAAATAT TCTGGTACCC TGAAAACGAC CGAAATCTAG AGAAACACTT CCTTGGAATG AAGACACCAC ACTGTATTAA

      5140        5150        5160        5170        5180        5190        5200        5210        5220
GGACAAACTA CCTACAGAGA TTTAAAGCTC TAAGGTAAAT ATAAAATTTT TAAGTGTATA ATGTGTTAAA CTACTGATTC TAATTGTTTG
CCTGTTTGAT GGATGTCTCT AAATTTCGAG ATTCCATTTA TATTTTAAAA ATTCACATAT TACACAATTT GATGACTAAG ATTAACAAAC

      5230        5240        5250        5260        5270        5280        5290        5300        5310
TGTATTTTAG ATTCCAACCT ATGGAACTGA TGAATGGGAG CAGTGGTGGA ATGCCTTTAA TGAGGAAAAC CTGTTTTGCT CAGAAGAAAT
ACATAAAATC TAAGGTTGGA TACCTTGACT ACTTACCCTC GTCACCACCT TACGGAAATT ACTCCTTTTG GACAAAACGA GTCTTCTTTA

      5320        5330        5340        5350        5360        5370        5380        5390        5400
GCCATCTAGT GATGATGAGG CTACTGCTGA CTCTCAACAT TCTACTCCTC CAAAAAAGAA GAGAAAGGTA GAAGACCCCA AGGACTTTCC
CGGTAGATCA CTACTACTCC GATGACGACT GAGAGTTGTA AGATGAGGAG GTTTTTTCTT CTCTTTCCAT CTTCTGGGGT TCCTGAAAGG
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Figure 14 (continued)

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      5410        5420        5430        5440        5450        5460        5470        5480        5490
TTCAGAATTG CTAAGTTTTT TGAGTCATGC TGTGTTTAGT AATAGAACTC TTGCTTGCTT TGCTATTTAC ACCACAAAGG AAAAAGCTGC
AAGTCTTAAC GATTCAAAAA ACTCAGTACG ACACAAATCA TTATCTTGAG AACGAACGAA ACGATAAATG TGGTGTTTCC TTTTTCGACG

      5500        5510        5520        5530        5540        5550        5560        5570        5580
ACTGCTATAC AAGAAAATTA TGGAAAAATA TTCTGTAACC TTTATAAGTA GGCATAACAG TTATAATCAT AACATACTGT TTTTTCTTAC
TGACGATATG TTCTTTTAAT ACCTTTTTAT AAGACATTGG AAATATTCAT CCGTATTGTC AATATTAGTA TTGTATGACA AAAAAGAATG

      5590        5600        5610        5620        5630        5640        5650        5660        5670
TCCACACAGG CATAGAGTGT CTGCTATTAA TAACTATGCT CAAAAATTGT GTACCTTTAG CTTTTTAATT TGTAAAGGGG TTAATAAGGA
AGGTGTGTCC GTATCTCACA GACGATAATT ATTGATACGA GTTTTTAACA CATGGAAATC GAAAAATTAA ACATTTCCCC AATTATTCCT

      5680        5690        5700        5710        5720        5730        5740        5750        5760
ATATTTGATG TATAGTGCCT TGACTAGAGA TCATAATCAG CCATACCACA TTTGTAGAGG TTTTACTTGC TTTAAAAAAC CTCCCACACC
TATAAACTAC ATATCACGGA ACTGATCTCT AGTATTAGTC GGTATGGTGT AAACATCTCC AAAATGAACG AAATTTTTTG GAGGGTGTGG

      5770        5780        5790        5800        5810        5820        5830        5840        5850
TCCCCCTGAA CCTGAAACAT AAAATGAATG CAATTGTTGT TGTTAACTTG TTTATTGCAG CTTATAATGG TTACAAATAA AGCAATAGCA
AGGGGGACTT GGACTTTGTA TTTTACTTAC GTTAACAACA ACAATTGAAC AAATAACGTC GAATATTACC AATGTTTATT TCGTTATCGT

      5860        5870        5880        5890        5900        5910        5920        5930        5940
TCACAAATTT CACAAATAAA GCATTTTTTT CACTGCATTC TAGTTGTGGT TTGTCCAAAC TCATCAATGT ATCTTATCAT GTCTGGATCG
AGTGTTTAAA GTGTTTATTT CGTAAAAAAA GTGACGTAAG ATCAACACCA AACAGGTTTG AGTAGTTACA TAGAATAGTA CAGACCTAGC

      5950        5960        5970        5980        5990        6000        6010        6020        6030
GCTGGATGAT CCTCCAGCGC GGGGATCTCA TGCTGGAGTT CTTCGCCCAC CCCAACTTGT TTATTGCAGC TTATAATGGT TACAAATAAA
CGACCTACTA GGAGGTCGCG CCCCTAGAGT ACGACCTCAA GAAGCGGGTG GGGTTGAACA AATAACGTCG AATATTACCA ATGTTTATTT

      6040        6050        6060        6070        6080        6090        6100        6110        6120
GCAATAGCAT CACAAATTTC ACAAATAAAG CATTTTTTTC ACTGCATTCT AGTTGTGGTT TGTCCAAACT CATCAATGTA TCTTATCATG
CGTTATCGTA GTGTTTAAAG TGTTTATTTC GTAAAAAAAG TGACGTAAGA TCAACACCAA ACAGGTTTGA GTAGTTACAT AGAATAGTAC

      6130        6140        6150        6160        6170        6180        6190        6200        6210
TCTGTATACC GTCGACCTCT AGCTAGAGCT TGGCGTAATC ATGGTCATAG CTGTTTCCTG TGTGAAATTG TTATCCGCTC ACAATTCCAC
AGACATATGG CAGCTGGAGA TCGATCTCGA ACCGCATTAG TACCAGTATC GACAAAGGAC ACACTTTAAC AATAGGCGAG TGTTAAGGTG

      6220        6230        6240        6250        6260        6270        6280        6290        6300
ACAACATACG AGCCGGAAGC ATAAAGTGTA AAGCCTGGGG TGCCTAATGA GTGAGCTAAC TCACATTAAT TGCGTTGCGC TCACTGCCCG
TGTTGTATGC TCGGCCTTCG TATTTCACAT TTCGGACCCC ACGGATTACT CACTCGATTG AGTGTAATTA ACGCAACGCG AGTGACGGGC
```

Figure 14
(continued)

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      6310       6320       6330       6340       6350       6360       6370       6380       6390
CTTTCCAGTC GGGAAACCTG TCGTGCCAGC TGCATTAATG AATCGGCCAA CGCGCGGGGA GAGGCGGTTT GCGTATTGGG CGCTCTTCCG
GAAAGGTCAG CCCTTTGGAC AGCACGGTCG ACGTAATTAC TTAGCCGGTT GCGCGCCCCT CTCCGCCAAA CGCATAACCC GCGAGAAGGC

      6400       6410       6420       6430       6440       6450       6460       6470       6480
CTTCCTCGCT CACTGACTCG CTGCGCTCGG TCGTTCGGCT GCGGCGAGCG GTATCAGCTC ACTCAAAGGC GGTAATACGG TTATCCACAG
GAAGGAGCGA GTGACTGAGC GACGCGAGCC AGCAAGCCGA CGCCGCTCGC CATAGTCGAG TGAGTTTCCG CCATTATGCC AATAGGTGTC

      6490       6500       6510       6520       6530       6540       6550       6560       6570
AATCAGGGGA TAACGCAGGA AAGAACATGT GAGCAAAAGG CCAGCAAAAG GCCAGGAACC GTAAAAAGGC CGCGTTGCTG GCGTTTTTCC
TTAGTCCCCT ATTGCGTCCT TTCTTGTACA CTCGTTTTCC GGTCGTTTTC CGGTCCTTGG CATTTTTCCG GCGCAACGAC CGCAAAAAGG

      6580       6590       6600       6610       6620       6630       6640       6650       6660
ATAGGCTCCG CCCCCCTGAC GAGCATCACA AAAATCGACG CTCAAGTCAG AGGTGGCGAA ACCCGACAGG ACTATAAAGA TACCAGGCGT
TATCCGAGGC GGGGGGACTG CTCGTAGTGT TTTTAGCTGC GAGTTCAGTC TCCACCGCTT TGGGCTGTCC TGATATTTCT ATGGTCCGCA

      6670       6680       6690       6700       6710       6720       6730       6740       6750
TTCCCCCTGG AAGCTCCCTC GTGCGCTCTC CTGTTCCGAC CCTGCCGCTT ACCGGATACC TGTCCGCCTT TCTCCCTTCG GGAAGCGTGG
AAGGGGGACC TTCGAGGGAG CACGCGAGAG GACAAGGCTG GGACGGCGAA TGGCCTATGG ACAGGCGGAA AGAGGGAAGC CCTTCGCACC

      6760       6770       6780       6790       6800       6810       6820       6830       6840
CGCTTTCTCA ATGCTCACGC TGTAGGTATC TCAGTTCGGT GTAGGTCGTT CGCTCCAAGC TGGGCTGTGT GCACGAACCC CCCGTTCAGC
GCGAAAGAGT TACGAGTGCG ACATCCATAG AGTCAAGCCA CATCCAGCAA GCGAGGTTCG ACCCGACACA CGTGCTTGGG GGGCAAGTCG

      6850       6860       6870       6880       6890       6900       6910       6920       6930
CCGACCGCTG CGCCTTATCC GGTAACTATC GTCTTGAGTC CAACCCGGTA AGACACGACT TATCGCCACT GGCAGCAGCC ACTGGTAACA
GGCTGGCGAC GCGGAATAGG CCATTGATAG CAGAACTCAG GTTGGGCCAT TCTGTGCTGA ATAGCGGTGA CCGTCGTCGG TGACCATTGT

      6940       6950       6960       .6970      6980       6990       7000       7010       7020
GGATTAGCAG AGCGAGGTAT GTAGGCGGTG CTACAGAGTT CTTGAAGTGG TGGCCTAACT ACGGCTACAC TAGAAGGACA GTATTTGGTA
CCTAATCGTC TCGCTCCATA CATCCGCCAC GATGTCTCAA GAACTTCACC ACCGGATTGA TGCCGATGTG ATCTTCCTGT CATAAACCAT

      7030       7040       7050       7060       7070       7080       7090       7100       7110
TCTGCGCTCT GCTGAAGCCA GTTACCTTCG GAAAAAGAGT TGGTAGCTCT TGATCCGGCA AACAAACCAC CGCTGGTAGC GGTGGTTTTT
AGACGCGAGA CGACTTCGGT CAATGGAAGC CTTTTTCTCA ACCATCGAGA ACTAGGCCGT TTGTTTGGTG GCGACCATCG CCACCAAAAA

      7120       7130       7140       7150       7160       7170       7180       7190       7200
TTGTTTGCAA GCAGCAGATT ACGCGCAGAA AAAAAGGATC TCAAGAAGAT CCTTTGATCT TTTCTACGGG GTCTGACGCT CAGTGGAACG
AACAAACGTT CGTCGTCTAA TGCGCGTCTT TTTTTCCTAG AGTTCTTCTA GGAAACTAGA AAAGATGCCC CAGACTGCGA GTCACCTTGC
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Figure 14
(continued)

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      7210       7220       7230       7240       7250       7260       7270       7280       7290
AAAACTCACG TTAAGGGATT TTGGTCATGA GATTATCAAA AAGGATCTTC ACCTAGATCC TTTTAAATTA AAAATGAAGT TTTAAATCAA
TTTTGAGTGC AATTCCCTAA AACCAGTACT CTAATAGTTT TTCCTAGAAG TGGATCTAGG AAAATTTAAT TTTTACTTCA AAATTTAGTT

      7300       7310       7320       7330       7340       7350       7360       7370       7380
TCTAAAGTAT ATATGAGTAA ACTTGGTCTG ACAGTTACCA ATGCTTAATC AGTGAGGCAC CTATCTCAGC GATCTGTCTA TTTCGTTCAT
AGATTTCATA TATACTCATT TGAACCAGAC TGTCAATGGT TACGAATTAG TCACTCCGTG GATAGAGTCG CTAGACAGAT AAAGCAAGTA

      7390       7400       7410       7420       7430       7440       7450       7460       7470
CCATAGTTGC CTGACTCCCC GTCGTGTAGA TAACTACGAT ACGGGAGGGC TTACCATCTG GCCCCAGTGC TGCAATGATA CCGCGAGACC
GGTATCAACG GACTGAGGGG CAGCACATCT ATTGATGCTA TGCCCTCCCG AATGGTAGAC CGGGGTCACG ACGTTACTAT GGCGCTCTGG

      7480       7490       7500       7510       7520       7530       7540       7550       7560
CACGCTCACC GGCTCCAGAT TTATCAGCAA TAAACCAGCC AGCCGGAAGG GCCGAGCGCA GAAGTGGTCC TGCAACTTTA TCCGCCTCCA
GTGCGAGTGG CCGAGGTCTA AATAGTCGTT ATTTGGTCGG TCGGCCTTCC CGGCTCGCGT CTTCACCAGG ACGTTGAAAT AGGCGGAGGT

      7570       7580       7590       7600       7610       7620       7630       7640       7650
TCCAGTCTAT TAATTGTTGC CGGGAAGCTA GAGTAAGTAG TTCGCCAGTT AATAGTTTGC GCAACGTTGT TGCCATTGCT ACAGGCATCG
AGGTCAGATA ATTAACAACG GCCCTTCGAT CTCATTCATC AAGCGGTCAA TTATCAAACG CGTTGCAACA ACGGTAACGA TGTCCGTAGC

      7660       7670       7680       7690       7700       7710       7720       7730       7740
TGGTGTCACG CTCGTCGTTT GGTATGGCTT CATTCAGCTC CGGTTCCCAA CGATCAAGGC GAGTTACATG ATCCCCCATG TTGTGCAAAA
ACCACAGTGC GAGCAGCAAA CCATACCGAA GTAAGTCGAG GCCAAGGGTT GCTAGTTCCG CTCAATGTAC TAGGGGGTAC AACACGTTTT

      7750       7760       7770       7780       7790       7800       7810       7820       7830
AAGCGGTTAG CTCCTTCGGT CCTCCGATCG TTGTCAGAAG TAAGTTGGCC GCAGTGTTAT CACTCATGGT TATGGCAGCA CTGCATAATT
TTCGCCAATC GAGGAAGCCA GGAGGCTAGC AACAGTCTTC ATTCAACCGG CGTCACAATA GTGAGTACCA ATACCGTCGT GACGTATTAA

      7840       7850       7860       7870       7880       7890       7900       7910       7920
CTCTTACTGT CATGCCATCC GTAAGATGCT TTTCTGTGAC TGGTGAGTAC TCAACCAAGT CATTCTGAGA ATAGTGTATG CGGCGACCGA
GAGAATGACA GTACGGTAGG CATTCTACGA AAAGACACTG ACCACTCATG AGTTGGTTCA GTAAGACTCT TATCACATAC GCCGCTGGCT

      7930       7940       7950       7960       7970       7980       7990       8000       8010
GTTGCTCTTG CCCGGCGTCA ATACGGGATA ATACCGCGCC ACATAGCAGA ACTTTAAAAG TGCTCATCAT TGGAAAACGT TCTTCGGGGC
CAACGAGAAC GGGCCGCAGT TATGCCCTAT TATGGCGCGG TGTATCGTCT TGAAATTTTC ACGAGTAGTA ACCTTTTGCA AGAAGCCCCG

      8020       8030       8040       8050       8060       8070       8080       8090       8100
GAAAACTCTC AAGGATCTTA CCGCTGTTGA GATCCAGTTC GATGTAACCC ACTCGTGCAC CCAACTGATC TTCAGCATCT TTTACTTTCA
CTTTTGAGAG TTCCTAGAAT GGCGACAACT CTAGGTCAAG CTACATTGGG TGAGCACGTG GGTTGACTAG AAGTCGTAGA AAATGAAAGT
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Figure 14
(continued)

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      8110        8120        8130        8140        8150        8160        8170        8180        8190
CCAGCGTTTC TGGGTGAGCA AAAACAGGAA GGCAAAATGC CGCAAAAAAG GGAATAAGGG CGACACGGAA ATGTTGAATA CTCATACTCT
GGTCGCAAAG ACCCACTCGT TTTTGTCCTT CCGTTTTACG GCGTTTTTTC CCTTATTCCC GCTGTGCCTT TACAACTTAT GAGTATGAGA

      8200        8210        8220        8230        8240        8250        8260        8270        8280
TCCTTTTTCA ATATTATTGA AGCATTTATC AGGGTTATTG TCTCATGAGC GGATACATAT TTGAATGTAT TTAGAAAAAT AAACAAATAG
AGGAAAAAGT TATAATAACT TCGTAAATAG TCCCAATAAC AGAGTACTCG CCTATGTATA AACTTACATA AATCTTTTTA TTTGTTTATC

      8290        8300        8310        8320        8330
GGGTTCCGCG CACATTTCCC CGAAAAGTGC CACCTGACGT C
CCCAAGGCGC GTGTAAAGGG GCTTTTCACG GTGGACTGCA G
```

Figure 14
(continued)

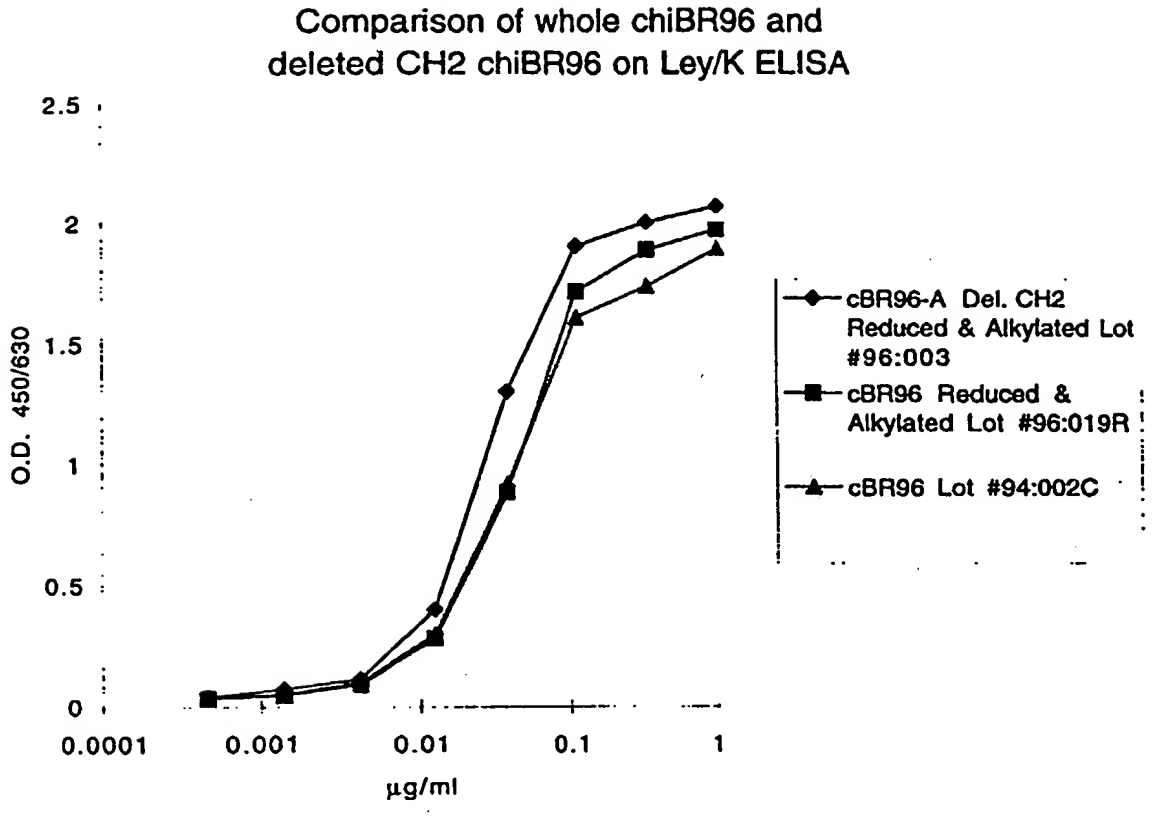

Comparison of whole chiBR96 and deleted CH2 chiBR96 on Ley/K ELISA
O.D. 450/630
2.5
2
1.5
1
0.5
0
0.0001
0.001
0.01
0.1
1
µg/ml
cBR96-A Del. CH2 Reduced & Alkylated Lot #96:003
cBR96 Reduced & Alkylated Lot #96:019R
cBR96 Lot #94:002C

Figure 15

hBR96-2B: L235 to A235 and G237 to A237

hBR96-2C: E318 to S318, K320 to S320, and K322 to S322

hBR96-2D: P331 to A331

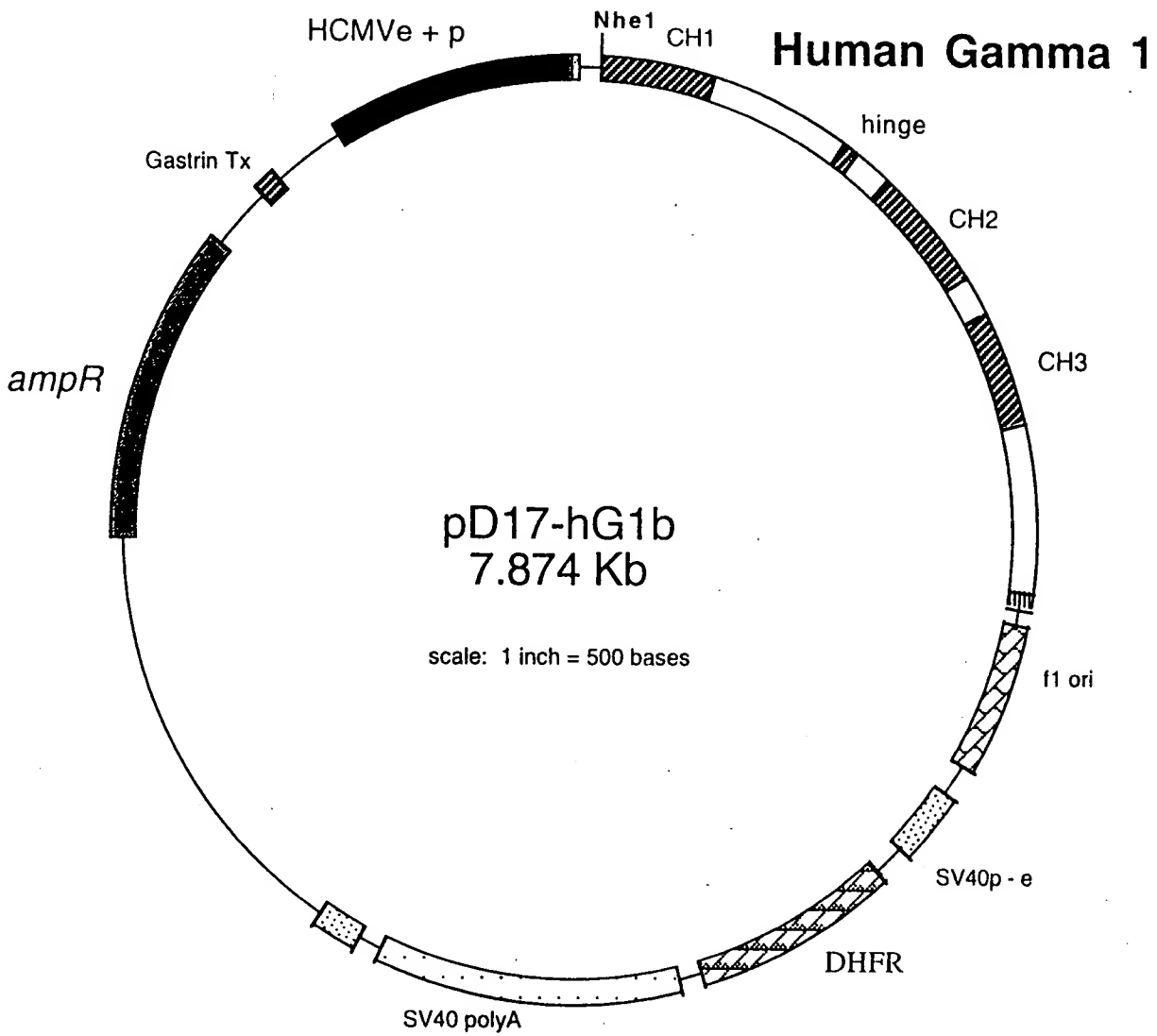
hBR96-2E: L235 to A235, G237 to A237, E318 to S318, K320 to S320, and K322 to S322

hBR96-2F: L235 to A235, G237 to A237, and P331 to A331

hBR96-2G: E318 to S318, K320 to S320, K322 to S322, and P331 to A331

hBR96-2H: L235 to A235, G237 to A237, E318 to S318, K320 to S320, K322 to S322, and P331 to A331

Figure 16


HCMVe + p
Nhe1
CH1
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hinge
CH2
CH3
Gastrin Tx
ampR
pD17-hG1b
7.874 Kb
scale: 1 inch = 500 bases
f1 ori
SV40p - e
DHFR
SV40 polyA

FIGURE 18A

1 GGTACCAATT TAAATTGATA TCTCCTTAGG TCTCGAGTCT CTAGATAACC
51 GGTCAATCGA TTGGAATTCT TGCGGCCGCT TGCTAGCCAC CATGGAGTTG
101 TGGTTAAGCT TGGTCTTCCT TGTCCTTGTT TTAAAAGGTG TCCAGTGTGA
151 AGTGCAACTG GTGGAGTCTG GGGGAGGCTT AGTGCAGCCT GGAGGGTCCC
201 TGCGACTTTC CTGTGCTGCA TCTGGATTCC CGTTCAGTGA CTATTACATG
251 TATTGGGTTC GCCAGGCTCC AGGCAAGGGA CTGGAGTGGG TCTCATACAT
301 TAGTCAAGAT GGTGATATAA CCGACTATGC AGACTCCGTA AAGGGTCGAT
351 TCACCATCTC CAGAGACAAT GCAAAGAACA GCCTGTACCT GCAAATGAAC
401 AGCCTGAGGG ACGAGGACAC AGCCGTGTAT TACTGTGCAA GAGGCCTGGC
451 GGACGGGGCC TGGTTTGCTT ACTGGGGCCA AGGGACTCTG GTCACGGTCT
501 CTTCCGCTAG CACCAAGGGC CCATCGGTCT TCCCCCTGGC ACCCTCCTCC
551 AAGAGCACCT CTGGGGGCAC AGCGGCCCTG GGCTGCCTGG TCAAGGACTA
601 CTTCCCCGAA CCGGTGACGG TGTCGTGGAA CTCAGGCGCC CTGACCAGCG
651 GCGTGCACAC CTTCCCGGCT GTCCTACAGT CCTCAGGACT CTACTCCCTC
701 AGCAGCGTGG TCACCGTGCC CTCCAGCAGC TTGGGCACCC AGACCTACAT
751 CTGCAACGTG AATCACAAGC CCAGCAACAC CAAGGTGGAC AAGAAAGTTG
801 GTGAGAGGCC AGCACAGGGA GGGAGGGTGT CTGCTGGAAG CCAGGCTCAG
851 CGCTCCTGCC TGGACGCATC CCGGCTATGC AGCCCCAGTC CAGGGCAGCA
901 AGGCAGGCCC CGTCTGCCTC TTCACCCGGA GGCCTCTGCC CGCCCCACTC
951 ATGCTCAGGG AGAGGGTCTT CTGGCTTTTT CCCCAGGCTC TGGGCAGGCA
1001 CAGGCTAGGT GCCCCTAACC CAGGCCCTGC ACACAAAGGG GCAGGTGCTG
1051 GGCTCAGACC TGCCAAGAGC CATATCCGGG AGGACCCTGC CCCTGACCTA
1101 AGCCCACCCC AAAGGCCAAA CTCTCCACTC CCTCAGCTCG GACACCTTCT
1151 CTCCTCCCAG ATTCCAGTAA CTCCCAATCT TCTCTCTGCA GAGCCCAAAT
1201 CTTGTGACAA AACTCACACA TGCCCACCGT GCCCAGGTAA GCCAGCCCAG
1251 GCCTCGCCCT CCAGCTCAAG GCGGGACAGG TGCCCTAGAG TAGCCTGCAT
1301 CCAGGGACAG GCCCCAGCCG GGTGCTGACA CGTCCACCTC CATCTCTTCC

```
                                  235                 237
1351  TCAGCACCTG AACTCCTGGG GGGACCGTCA GTCTTCCTCT TCCCCCCAAA
1401  ACCCAAGGAC ACCCTCATGA TCTCCCGGAC CCCTGAGGTC ACATGCGTGG
1451  TGGTGGACGT GAGCCACGAA GACCCTGAGG TCAAGTTCAA CTGGTACGTG
1501  GACGGCGTGG AGGTGCATAA TGCCAAGACA AAGCCGCGGG AGGAGCAGTA
1551  CAACAGCACG TACCGTGTGG TCAGCGTCCT CACCGTCCTG CACCAGGACT
                    318                 320     322
1601  GGCTGAATGG CAAGGAGTAC AAGTGCAAGG TCTCCAACAA AGCCCTCCCA
          331
1651  GCCCCCATCG AGAAAACCAT CTCCAAAGCC AAAGGTGGGA CCCGTGGGGT
1701  GCGAGGGCCA CATGGACAGA GGCCGGCTCG GCCCACCCTC TGCCCTGAGA
1751  GTGACCGCTG TACCAACCTC TGTCCCTACA GGGCAGCCCC GAGAACCACA
1801  GGTGTACACC CTGCCCCCAT CCCGGGATGA GCTGACCAAG AACCAGGTCA
1851  GCCTGACCTG CCTGGTCAAA GGCTTCTATC CCAGCGACAT CGCCGTGGAG
1901  TGGGAGAGCA ATGGGCAGCC GGAGAACAAC TACAAGACCA CGCCTCCCGT
1951  GCTGGACTCC GACGGCTCCT TCTTCCTCTA CAGCAAGCTC ACCGTGGACA
2001  AGAGCAGGTG GCAGCAGGGG AACGTCTTCT CATGCTCCGT GATGCATGAG
2051  GCTCTGCACA ACCACTACAC GCAGAAGAGC CTCTCCCTGT CTCCGGGTAA
2101  ATGAGTGCGA CGGCCGGCAA GCCCCCGCTC CCCGGGCTCT CGCGGTCGCA
2151  CGAGGATGCT TGGCACGTAC CCCCTGTACA TACTTCCCGG GCGCCCAGCA
2201  TGGAAATAAA GCACCCAGCG CTGCCCTGGG CCCCTGCGAG ACTGTGATGG
2251  TTCTTTCCAC GGGTCAGGCC GAGTCTGAGG CCTGAGTGGC ATGAGGGAGG
2301  CAGAGCGGGT CCCACTGTCC CCACACTGGC CCAGGCTGTG CAGGTGTGCC
2351  TGGGCCCCCT AGGGTGGGGC TCAGCCAGGG GCTGCCCTCG GCAGGGTGGG
2401  GGATTTGCCA GCGTGGCCCT CCCTCCAGCA GCACCTGCCC TGGGCTGGGC
2451  CACGGGAAGC CCTAGGAGCC CCTGGGGACA GACACACAGC CCCTGCCTCT
2501  GTAGGAGACT GTCCTGTTCT GTGAGCGCCC CTGTCCTCCC GACCTCCATG
2551  CCCACTCGGG GGCATGCCTA GTCCATGTGC GTAGGGACAG GCCCTCCCTC
2601  ACCCATCTAC CCCCACGGCA CTAACCCCTG GCTGCCCTGC CCAGCCTCGC
2651  ACCCGCATGG GGACACAACC GACTCCGGGG ACATGCACTC TCGGGCCCTG
2701  TGGAGGGACT GGTGCAGATG CCCACACACA CACTCAGCCC AGACCCGTTC
2751  AACAAACCCC GCACTGAGGT TGGCCGGCCA CACGGCCACC ACACACACAC
2801  GTGCACGCCT CACACACGGA GCCTCACCCG GGCGAACTGC ACAGCACCCA
```


FIGURE 18B

2851 GACCAGAGCA AGGTCCTCGC ACACGTGAAC ACTCCTCGGA CACAGGCCCC

2901 CACGAGCCCC ACGCGGCACC TCAAGGCCCA CGAGCCTCTC GGCAGCTTCT

2951 CCACATGCTG ACCTGCTCAG ACAAACCCAG CCCTCCTCTC ACAAGGGTGC

3001 CCCTGCAGCC GCCACACACA CACAGGGGAT CACACACCAC GTCACGTCCC

3051 TGGCCCTGGC CCACTTCCCA GTGCCGCCCT TCCCTGCAGG ACGGATCAGC

3101 CTCGACTGTG CCTTCTAGTT GCCAGCCATC TGTTGTTTGC CCCTCCCCCG

3151 TGCCTTCCTT GACCCTGGAA GGTGCCACTC CCACTGTCCT TTCCTAATAA

3201 AATGAGGAAA TTGCATCGCA TTGTCTGAGT AGGTGTCATT CTATTCTGGG

3251 GGGTGGGGTG GGGCAGGACA GCAAGGGGGA GGATTGGGAA GACAATAGCA

3301 GGCATGCTGG GGATGCGGTG GGCTCTATGG CTTCTGAGGC GGAAAGAACC

3351 AGCTGGGGCT CTAGGGGGTA TCCCCACGCG CCCTGTAGCG GCGCATTAAG

3401 CGCGGCGGGT GTGGTGGTTA CGCGCAGCGT GACCGCTACA CTTGCCAGCG

3451 CCCTAGCGCC CGCTCCTTTC GCTTTCTTCC CTTCCTTTCT CGCCACGTTC

3501 GCCGGGCCTC TCAAAAAAGG GAAAAAAAGC ATGCATCTCA ATTAGTCAGC

3551 AACCATAGTC CCGCCCCTAA CTCCGCCCAT CCCGCCCCTA ACTCCGCCCA

3601 GTTCCGCCCA TTCTCCGCCC CATGGCTGAC TAATTTTTTT TATTTATGCA

3651 GAGGCCGAGG CCGCCTCGGC CTCTGAGCTA TTCCAGAAGT AGTGAGGAGG

3701 CTTTTTTGGA GGCCTAGGCT TTTGCAAAAA GCTTGGACAG CTCAGGGCTG

3751 CGATTTCGCG CCAAACTTGA CGGCAATCCT AGCGTGAAGG CTGGTAGGAT

3801 TTTATCCCCG CTGCCATCAT GGTTCGACCA TTGAACTGCA TCGTCGCCGT

3851 GTCCCAAAAT ATGGGGATTG GCAAGAACGG AGACCTACCC TGGCCTCCGC

3901 TCAGGAACGA GTTCAAGTAC TTCCAAAGAA TGACCACAAC CTCTTCAGTG

3951 GAAGGTAAAC AGAATCTGGT GATTATGGGT AGGAAAACCT GGTTCTCCAT

4001 TCCTGAGAAG AATCGACCTT TAAAGGACAG AATTAATATA GTTCTCAGTA

4051 GAGAACTCAA AGAACCACCA CGAGGAGCTC ATTTTCTTGC CAAAAGTTTG

4101 GATGATGCCT TAAGACTTAT TGAACAACCG GAATTGGCAA GTAAAGTAGA

4151 CATGGTTTGG ATAGTCGGAG GCAGTTCTGT TTACCAGGAA GCCATGAATC

4201 AACCAGGCCA CCTTAGACTC TTTGTGACAA GGATCATGCA GGAATTTGAA

4251 AGTGACACGT TTTTCCCAGA AATTGATTTG GGGAAATATA AACTTCTCCC

4301 AGAATACCCA GGCGTCCTCT CTGAGGTCCA GGAGGAAAAA GGCATCAAGT

FIGURE 18C

4351 ATAAGTTTGA AGTCTACGAG AAGAAAGACT AACAGGAAGA TGCTTTCAAG

4401 TTCTCTGCTC CCCTCCTAAA GCTATGCATT TTTATAAGAC CATGGGACTT

4451 TTGCTGGCTT TAGATCTCTT TGTGAAGGAA CCTTACTTCT GTGGTGTGAC

4501 ATAATTGGAC AAACTACCTA CAGAGATTTA AAGCTCTAAG GTAAATATAA

4551 AATTTTTAAG TGTATAATGT GTTAAACTAC TGATTCTAAT TGTTTGTGTA

4601 TTTTAGATTC CAACCTATGG AACTGATGAA TGGGAGCAGT GGTGGAATGC

4651 CTTTAATGAG GAAAACCTGT TTTGCTCAGA AGAAATGCCA TCTAGTGATG

4701 ATGAGGCTAC TGCTGACTCT CAACATTCTA CTCCTCCAAA AAAGAAGAGA

4751 AAGGTAGAAG ACCCCAAGGA CTTTCCTTCA GAATTGCTAA GTTTTTTGAG

4801 TCATGCTGTG TTTAGTAATA GAACTCTTGC TTGCTTTGCT ATTTACACCA

4851 CAAAGGAAAA AGCTGCACTG CTATACAAGA AAATTATGGA AAAATATTCT

4901 GTAACCTTTA TAAGTAGGCA TAACAGTTAT AATCATAACA TACTGTTTTT

4951 TCTTACTCCA CACAGGCATA GAGTGTCTGC TATTAATAAC TATGCTCAAA

5001 AATTGTGTAC CTTTAGCTTT TTAATTTGTA AAGGGGTTAA TAAGGAATAT

5051 TTGATGTATA GTGCCTTGAC TAGAGATCAT AATCAGCCAT ACCACATTTG

5101 TAGAGGTTTT ACTTGCTTTA AAAAACCTCC CACACCTCCC CCTGAACCTG

5151 AAACATAAAA TGAATGCAAT TGTTGTTGTT AACTTGTTTA TTGCAGCTTA

5201 TAATGGTTAC AAATAAAGCA ATAGCATCAC AAATTTCACA AATAAAGCAT

5251 TTTTTTCACT GCATTCTAGT TGTGGTTTGT CCAAACTCAT CAATGTATCT

5301 TATCATGTCT GGATCGGCTG GATGATCCTC CAGCGCGGGG ATCTCATGCT

5351 GGAGTTCTTC GCCCACCCCA ACTTGTTTAT TGCAGCTTAT AATGGTTACA

5401 AATAAAGCAA TAGCATCACA AATTTCACAA ATAAAGCATT TTTTTCACTG

5451 CATTCTAGTT GTGGTTTGTC CAAACTCATC AATGTATCTT ATCATGTCTG

5501 TATACCGTCG ACCTCTAGCT AGAGCTTGGC GTAATCATGG TCATAGCTGT

5551 TTCCTGTGTG AAATTGTTAT CCGCTCACAA TTCCACACAA CATACGAGCC

5601 GGAAGCATAA AGTGTAAAGC CTGGGGTGCC TAATGAGTGA GCTAACTCAC

5651 ATTAATTGCG TTGCGCTCAC TGCCCGCTTT CCAGTCGGGA AACCTGTCGT

5701 GCCAGCTGCA TTAATGAATC GGCCAACGCG CGGGGAGAGG CGGTTTGCGT

5751 ATTGGGCGCT CTTCCGCTTC CTCGCTCACT GACTCGCTGC GCTCGGTCGT

5801 TCGGCTGCGG CGAGCGGTAT CAGCTCACTC AAAGGCGGTA ATACGGTTAT

FIGURE 18D

5351 CCACAGAATC AGGGGATAAC GCAGGAAAGA ACATGTGAGC AAAAGGCCAG

5901 CAAAAGGCCA GGAACCGTAA AAAGGCCGCG TTGCTGGCGT TTTTCCATAG

5951 GCTCCGCCCC CCTGACGAGC ATCACAAAAA TCGACGCTCA AGTCAGAGGT

6001 GGCGAAACCC GACAGGACTA TAAAGATACC AGGCGTTTCC CCCTGGAAGC

6051 TCCCTCGTGC GCTCTCCTGT TCCGACCCTG CCGCTTACCG GATACCTGTC

6101 CGCCTTTCTC CCTTCGGGAA GCGTGGCGCT TTCTCAATGC TCACGCTGTA

6151 GGTATCTCAG TTCGGTGTAG GTCGTTCGCT CCAAGCTGGG CTGTGTGCAC

6201 GAACCCCCCG TTCAGCCCGA CCGCTGCGCC TTATCCGGTA ACTATCGTCT

6251 TGAGTCCAAC CCGGTAAGAC ACGACTTATC GCCACTGGCA GCAGCCACTG

6301 GTAACAGGAT TAGCAGAGCG AGGTATGTAG GCGGTGCTAC AGAGTTCTTG

6351 AAGTGGTGGC CTAACTACGG CTACACTAGA AGGACAGTAT TTGGTATCTG

6401 CGCTCTGCTG AAGCCAGTTA CCTTCGGAAA AAGAGTTGGT AGCTCTTGAT

6451 CCGGCAAACA AACCACCGCT GGTAGCGGTG GTTTTTTTGT TTGCAAGCAG

6501 CAGATTACGC GCAGAAAAAA AGGATCTCAA GAAGATCCTT TGATCTTTTC

6551 TACGGGGTCT GACGCTCAGT GGAACGAAAA CTCACGTTAA GGGATTTTGG

6601 TCATGAGATT ATCAAAAAGG ATCTTCACCT AGATCCTTTT AAATTAAAAA

6651 TGAAGTTTTA AATCAATCTA AAGTATATAT GAGTAAACTT GGTCTGACAG

6701 TTACCAATGC TTAATCAGTG AGGCACCTAT CTCAGCGATC TGTCTATTTC

6751 GTTCATCCAT AGTTGCCTGA CTCCCCGTCG TGTAGATAAC TACGATACGG

6801 GAGGGCTTAC CATCTGGCCC CAGTGCTGCA ATGATACCGC GAGACCCACG

6851 CTCACCGGCT CCAGATTTAT CAGCAATAAA CCAGCCAGCC GGAAGGGCCG

6901 AGCGCAGAAG TGGTCCTGCA ACTTTATCCG CCTCCATCCA GTCTATTAAT

6951 TGTTGCCGGG AAGCTAGAGT AAGTAGTTCG CCAGTTAATA GTTTGCGCAA

7001 CGTTGTTGCC ATTGCTACAG GCATCGTGGT GTCACGCTCG TCGTTTGGTA

7051 TGGCTTCATT CAGCTCCGGT TCCCAACGAT CAAGGCGAGT TACATGATCC

7101 CCCATGTTGT GCAAAAAAGC GGTTAGCTCC TTCGGTCCTC CGATCGTTGT

7151 CAGAAGTAAG TTGGCCGCAG TGTTATCACT CATGGTTATG GCAGCACTGC

7201 ATAATTCTCT TACTGTCATG CCATCCGTAA GATGCTTTTC TGTGACTGGT

7251 GAGTACTCAA CCAAGTCATT CTGAGAATAG TGTATGCGGC GACCGAGTTG

7301 CTCTTGCCCG GCGTCAATAC GGGATAATAC CGCGCCACAT AGCAGAACTT

FIGURE 18E

7351 TAAAAGTGCT CATCATTGGA AAACGTTCTT CGGGGCGAAA ACTCTCAAGG

7401 ATCTTACCGC TGTTGAGATC CAGTTCGATG TAACCCACTC GTGCACCCAA

7451 CTGATCTTCA GCATCTTTTA CTTTCACCAG CGTTTCTGGG TGAGCAAAAA

7501 CAGGAAGGCA AAATGCCGCA AAAAAGGGAA TAAGGGCGAC ACGGAAATGT

7551 TGAATACTCA TACTCTTCCT TTTTCAATAT TATTGAAGCA TTTATCAGGG

7601 TTATTGTCTC ATGAGCGGAT ACATATTTGA ATGTATTTAG AAAAATAAAC

7651 AAATAGGGGT TCCGCGCACA TTTCCCCGAA AAGTGCCACC TGACGTCGAC

7701 GGATCGGGAG ATCTGCTAGG TGACCTGAGG CGCGCCGGCT TCGAATAGCC

7751 AGAGTAACCT TTTTTTTTAA TTTTATTTTA TTTTATTTTT GAGATGGAGT

7801 TTGGCGCCGA TCTCCCGATC CCCTATGGTC GACTCTCAGT ACAATCTGCT

7851 CTGATGCCGC ATAGTTAAGC CAGTATCTGC TCCCTGCTTG TGTGTTGGAG

7901 GTCGCTGAGT AGTGCGCGAG CAAAATTTAA GCTACAACAA GGCAAGGCTT

7951 GACCGACAAT TGCATGAAGA ATCTGCTTAG GGTTAGGCGT TTTGCGCTGC

8001 TTCGCGATGT ACGGGCCAGA TATACGCGTT GACATTGATT ATTGACTAGT

8051 TATTAATAGT AATCAATTAC GGGGTCATTA GTTCATAGCC CATATATGGA

8101 GTTCCGCGTT ACATAACTTA CGGTAAATGG CCCGCCTGGC TGACCGCCCA

8151 ACGACCCCCG CCCATTGACG TCAATAATGA CGTATGTTCC CATAGTAACG

8201 CCAATAGGGA CTTTCCATTG ACGTCAATGG GTGGACTATT TACGGTAAAC

8251 TGCCCACTTG GCAGTACATC AAGTGTATCA TATGCCAAGT ACGCCCCCTA

8301 TTGACGTCAA TGACGGTAAA TGGCCCGCCT GGCATTATGC CCAGTACATG

8351 ACCTTATGGG ACTTTCCTAC TTGGCAGTAC ATCTACGTAT TAGTCATCGC

8401 TATTACCATG GTGATGCGGT TTTGGCAGTA CATCAATGGG CGTGGATAGC

8451 GGTTTGACTC ACGGGGATTT CCAAGTCTCC ACCCCATTGA CGTCAATGGG

8501 AGTTTGTTTT GGCACCAAAA TCAACGGGAC TTTCCAAAAT GTCGTAACAA

8551 CTCCGCCCCA TTGACGCAAA TGGGCGGTAG GCGTGTACGG TGGGAGGTCT

8601 ATATAAGCAG AGCTCTCTGG CTAACTAGAG AACCCACTGC TTACTGGCTT

8651 ATCGAAATTA ATACGACTCA CTATAGGGAG ACCCAAGCTT

FIGURE 18F

FIGURE 19 A

pD17-hG1b

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        10          20          30          40          50          60
GGTACCAATT TAAATTGATA TCTCCTTAGG TCTCGAGTCT CTAGATAACC GGTCAATCGA
CCATGGTTAA ATTTAACTAT AGAGGAATCC AGAGCTCAGA GATCTATTGG CCAGTTAGCT

        70          80          90          100         110         120
TTGGAATTCT TGCGGCCGCT TGCTAGCACC AAGGGCCCAT CGGTCTTCCC CCTGGCACCC
AACCTTAAGA ACGCCGGCGA ACGATCGTGG TTCCCGGGTA GCCAGAAGGG GGACCGTGGG

        130         140         150         160         170         180
TCCTCCAAGA GCACCTCTGG GGGCACAGCG GCCCTGGGCT GCCTGGTCAA GGACTACTTC
AGGAGGTTCT CGTGGAGACC CCCGTGTCGC CGGGACCCGA CGGACCAGTT CCTGATGAAG

        190         200         210         220         230         240
CCCGAACCGG TGACGGTGTC GTGGAACTCA GGCGCCCTGA CCAGCGGCGT GCACACCTTC
GGGCTTGGCC ACTGCCACAG CACCTTGAGT CCGCGGGACT GGTCGCCGCA CGTGTGGAAG

        250         260         270         280         290         300
CCGGCTGTCC TACAGTCCTC AGGACTCTAC TCCCTCAGCA GCGTGGTCAC CGTGCCCTCC
GGCCGACAGG ATGTCAGGAG TCCTGAGATG AGGGAGTCGT CGCACCAGTG GCACGGGAGG

        310         320         330         340         350         360
AGCAGCTTGG GCACCCAGAC CTACATCTGC AACGTGAATC ACAAGCCCAG CAACACCAAG
TCGTCGAACC CGTGGGTCTG GATGTAGACG TTGCACTTAG TGTTCGGGTC GTTGTGGTTC

        370         380         390         400         410         420
GTGGACAAGA AAGTTGGTGA GAGGCCAGCA CAGGGAGGGA GGGTGTCTGC TGGAAGCCAG
CACCTGTTCT TTCAACCACT CTCCGGTCGT GTCCCTCCCT CCCACAGACG ACCTTCGGTC

        430         440         450         460         470         480
GCTCAGCGCT CCTGCCTGGA CGCATCCCGG CTATGCAGCC CCAGTCCAGG GCAGCAAGGC
CGAGTCGCGA GGACGGACCT GCGTAGGGCC GATACGTCGG GGTCAGGTCC CGTCGTTCCG

        490         500         510         520         530         540
AGGCCCCGTC TGCCTCTTCA CCCGGAGGCC TCTGCCCGCC CCACTCATGC TCAGGGAGAG
TCCGGGGCAG ACGGAGAAGT GGGCCTCCGG AGACGGGCGG GGTGAGTACG AGTCCCTCTC

        550         560         570         580         590         600
GGTCTTCTGG CTTTTTCCCC AGGCTCTGGG CAGGCACAGG CTAGGTGCCC CTAACCCAGG
CCAGAAGACC GAAAAAGGGG TCCGAGACCC GTCCGTGTCC GATCCACGGG GATTGGGTCC
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FIGURE 19B

pD17-hG1b

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          610         620         630         640         650         660
CCCTGCACAC AAAGGGGCAG GTGCTGGGCT CAGACCTGCC AAGAGCCATA TCCGGGAGGA
GGGACGTGTG TTTCCCCGTC CACGACCCGA GTCTGGACGG TTCTCGGTAT AGGCCCTCCT

          670         680         690         700         710         720
CCCTGCCCCT GACCTAAGCC CACCCCAAAG GCCAAACTCT CCACTCCCTC AGCTCGGACA
GGGACGGGGA CTGGATTCGG GTGGGGTTTC CGGTTTGAGA GGTGAGGGAG TCGAGCCTGT

          730         740         750         760         770         780
CCTTCTCTCC TCCCAGATTC CAGTAACTCC CAATCTTCTC TCTGCAGAGC CCAAATCTTG
GGAAGAGAGG AGGGTCTAAG GTCATTGAGG GTTAGAAGAG AGACGTCTCG GGTTTAGAAC

          790         800         810         820         830         840
TGACAAAACT CACACATGCC CACCGTGCCC AGGTAAGCCA GCCCAGGCCT CGCCCTCCAG
ACTGTTTTGA GTGTGTACGG GTGGCACGGG TCCATTCGGT CGGGTCCGGA GCGGGAGGTC

          850         860         870         880         890         900
CTCAAGGCGG GACAGGTGCC CTAGAGTAGC CTGCATCCAG GGACAGGCCC CAGCCGGGTG
GAGTTCCGCC CTGTCCACGG GATCTCATCG GACGTAGGTC CCTGTCCGGG GTCGGCCCAC

          910         920         930         940  235    950 237     960
CTGACACGTC CACCTCCATC TCTTCCTCAG CACCTGAACT CCTGGGGGGA CCGTCAGTCT
GACTGTGCAG GTGGAGGTAG AGAAGGAGTC GTGGACTTGA GGACCCCCCT GGCAGTCAGA

          970         980         990         1000        1010        1020
TCCTCTTCCC CCCAAAACCC AAGGACACCC TCATGATCTC CCGGACCCCT GAGGTCACAT
AGGAGAAGGG GGGTTTTGGG TTCCTGTGGG AGTACTAGAG GGCCTGGGGA CTCCAGTGTA

          1030        1040        1050        1060        1070        1080
GCGTGGTGGT GGACGTGAGC CACGAAGACC CTGAGGTCAA GTTCAACTGG TACGTGGACG
CGCACCACCA CCTGCACTCG GTGCTTCTGG GACTCCAGTT CAAGTTGACC ATGCACCTGC

          1090        1100        1110        1120        1130        1140
GCGTGGAGGT GCATAATGCC AAGACAAAGC CGCGGGAGGA GCAGTACAAC AGCACGTACC
CGCACCTCCA CGTATTACGG TTCTGTTTCG GCGCCCTCCT CGTCATGTTG TCGTGCATGG
                                                          320
          1150        1160        1170        1180        1190 318    1200
GTGTGGTCAG CGTCCTCACC GTCCTGCACC AGGACTGGCT GAATGGCAAG GAGTACAAGT
CACACCAGTC GCAGGAGTGG CAGGACGTGG TCCTGACCGA CTTACCGTTC CTCATGTTCA
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FIGURE 19D

pD17-hG1b

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      1810        1820        1830        1840        1850        1860
CCTGGGCCCC TGCGAGACTG TGATGGTTCT TTCCACGGGT CAGGCCGAGT CTGAGGCCTG
GGACCCGGGG ACGCTCTGAC ACTACCAAGA AAGGTGCCCA GTCCGGCTCA GACTCCGGAC

      1870        1880        1890        1900        1910        1920
AGTGGCATGA GGGAGGCAGA GCGGGTCCCA CTGTCCCCAC ACTGGCCCAG GCTGTGCAGG
TCACCGTACT CCCTCCGTCT CGCCCAGGGT GACAGGGGTG TGACCGGGTC CGACACGTCC

      1930        1940        1950        1960        1970        1980
TGTGCCTGGG CCCCCTAGGG TGGGGCTCAG CCAGGGGCTG CCCTCGGCAG GGTGGGGGAT
ACACGGACCC GGGGGATCCC ACCCCGAGTC GGTCCCCGAC GGGAGCCGTC CCACCCCCTA

      1990        2000        2010        2020        2030        2040
TTGCCAGCGT GGCCCTCCCT CCAGCAGCAC CTGCCCTGGG CTGGGCCACG GGAAGCCCTA
AACGGTCGCA CCGGGAGGGA GGTCGTCGTG GACGGGACCC GACCCGGTGC CCTTCGGGAT

      2050        2060        2070        2080        2090        2100
GGAGCCCCTG GGGACAGACA CACAGCCCCT GCCTCTGTAG GAGACTGTCC TGTTCTGTGA
CCTCGGGGAC CCCTGTCTGT GTGTCGGGGA CGGAGACATC CTCTGACAGG ACAAGACACT

      2110        2120        2130        2140        2150        2160
GCGCCCCTGT CCTCCCGACC TCCATGCCCA CTCGGGGGCA TGCTGGGGAT GCGGTGGGCT
CGCGGGGACA GGAGGGCTGG AGGTACGGGT GAGCCCCCGT ACGACCCCTA CGCCACCCGA

      2170        2180        2190        2200        2210        2220
CTATGGCTTC TGAGGCGGAA AGAACCAGCT GGGGCTCTAG GGGGTATCCC CACGCGCCCT
GATACCGAAG ACTCCGCCTT TCTTGGTCGA CCCCGAGATC CCCCATAGGG GTGCGCGGGA

      2230        2240        2250        2260        2270        2280
GTAGCGGCGC ATTAAGCGCG GCGGGTGTGG TGGTTACGCG CAGCGTGACC GCTACACTTG
CATCGCCGCG TAATTCGCGC CGCCCACACC ACCAATGCGC GTCGCACTGG CGATGTGAAC

      2290        2300        2310        2320        2330        2340
CCAGCGCCCT AGCGCCCGCT CCTTTCGCTT TCTTCCCTTC CTTTCTCGCC ACGTTCGCCG
GGTCGCGGGA TCGCGGGCGA GGAAAGCGAA AGAAGGGAAG GAAAGAGCGG TGCAAGCGGC

      2350        2360        2370        2380        2390        2400
GCTTTCCCCG TCAAGCTCTA AATCGGGGCA TCCCTTTAGG GTTCCGATTT AGTGCTTTAC
CGAAAGGGGC AGTTCGAGAT TTAGCCCCGT AGGGAAATCC CAAGGCTAAA TCACGAAATG
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FIGURE 19C

pD17-hG1b

322 331

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      1210        1220        1230        1240        1250        1260
GCAAGGTCTC CAACAAAGCC CTCCCAGCCC CCATCGAGAA AACCATCTCC AAAGCCAAAG
CGTTCCAGAG GTTGTTTCGG GAGGGTCGGG GGTAGCTCTT TTGGTAGAGG TTTCGGTTTC

      1270        1280        1290        1300        1310        1320
GTGGGACCCG TGGGGTGCGA GGGCCACATG GACAGAGGCC GGCTCGGCCC ACCCTCTGCC
CACCCTGGGC ACCCCACGCT CCCGGTGTAC CTGTCTCCGG CCGAGCCGGG TGGGAGACGG

      1330        1340        1350        1360        1370        1380
CTGAGAGTGA CCGCTGTACC AACCTCTGTC CCTACAGGGC AGCCCCGAGA ACCACAGGTG
GACTCTCACT GGCGACATGG TTGGAGACAG GGATGTCCCG TCGGGGCTCT TGGTGTCCAC

      1390        1400        1410        1420        1430        1440
TACACCCTGC CCCCATCCCG GGATGAGCTG ACCAAGAACC AGGTCAGCCT GACCTGCCTG
ATGTGGGACG GGGGTAGGGC CCTACTCGAC TGGTTCTTGG TCCAGTCGGA CTGGACGGAC

      1450        1460        1470        1480        1490        1500
GTCAAAGGCT TCTATCCCAG CGACATCGCC GTGGAGTGGG AGAGCAATGG GCAGCCGGAG
CAGTTTCCGA AGATAGGGTC GCTGTAGCGG CACCTCACCC TCTCGTTACC CGTCGGCCTC

      1510        1520        1530        1540        1550        1560
AACAACTACA AGACCACGCC TCCCGTGCTG GACTCCGACG GCTCCTTCTT CCTCTACAGC
TTGTTGATGT TCTGGTGCGG AGGGCACGAC CTGAGGCTGC CGAGGAAGAA GGAGATGTCG

      1570        1580        1590        1600        1610        1620
AAGCTCACCG TGGACAAGAG CAGGTGGCAG CAGGGGAACG TCTTCTCATG CTCCGTGATG
TTCGAGTGGC ACCTGTTCTC GTCCACCGTC GTCCCCTTGC AGAAGAGTAC GAGGCACTAC

      1630        1640        1650        1660        1670        1680
CATGAGGCTC TGCACAACCA CTACACGCAG AAGAGCCTCT CCCTGTCTCC GGGTAAATGA
GTACTCCGAG ACGTGTTGGT GATGTGCGTC TTCTCGGAGA GGGACAGAGG CCCATTTACT

      1690        1700        1710        1720        1730        1740
GTGCGACGGC CGGCAAGCCC CCGCTCCCCG GGCTCTCGCG GTCGCACGAG GATGCTTGGC
CACGCTGCCG GCCGTTCGGG GGCGAGGGGC CCGAGAGCGC CAGCGTGCTC CTACGAACCG

      1750        1760        1770        1780        1790        1800
ACGTACCCCC TGTACATACT TCCCGGGCGC CCAGCATGGA AATAAAGCAC CCAGCGCTGC
TGCATGGGGG ACATGTATGA AGGGCCCGCG GGTCGTACCT TTATTTCGTG GGTCGCGACG
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FIGURE 19E

pD17-hG1b

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      2410        2420        2430        2440        2450        2460
GGCACCTCGA CCCCAAAAAA CTTGATTAGG GTGATGGTTC ACGTAGTGGG CCATCGCCCT
CCGTGGAGCT GGGGTTTTTT GAACTAATCC CACTACCAAG TGCATCACCC GGTAGCGGGA

      2470        2480        2490        2500        2510        2520
GATAGACGGT TTTTCGCCCT TTGACGTTGG AGTCCACGTT CTTTAATAGT GGACTCTTGT
CTATCTGCCA AAAAGCGGGA AACTGCAACC TCAGGTGCAA GAAATTATCA CCTGAGAACA

      2530        2540        2550        2560        2570        2580
TCCAAACTGG AACAACACTC AACCCTATCT CGGTCTATTC TTTTGATTTA TAAGGGATTT
AGGTTTGACC TTGTTGTGAG TTGGGATAGA GCCAGATAAG AAAACTAAAT ATTCCCTAAA

      2590        2600        2610        2620        2630        2640
TGGGGATTTC GGCCTATTGG TTAAAAAATG AGCTGATTTA ACAAAAATTT AACGCGAATT
ACCCCTAAAG CCGGATAACC AATTTTTTAC TCGACTAAAT TGTTTTTAAA TTGCGCTTAA

      2650        2660        2670        2680        2690        2700
AATTCTGTGG AATGTGTGTC AGTTAGGGTG TGGAAAGTCC CCAGGCTCCC CAGGCAGGCA
TTAAGACACC TTACACACAG TCAATCCCAC ACCTTTCAGG GGTCCGAGGG GTCCGTCCGT

      2710        2720        2730        2740        2750        2760
GAAGTATGCA AAGCATGCAT CTCAATTAGT CAGCAACCAT AGTCCCGCCC CTAACTCCGC
CTTCATACGT TTCGTACGTA GAGTTAATCA GTCGTTGGTA TCAGGGCGGG GATTGAGGCG

      2770        2780        2790        2800        2810        2820
CCATCCCGCC CCTAACTCCG CCCAGTTCCG CCCATTCTCC GCCCCATGGC TGACTAATTT
GGTAGGGCGG GGATTGAGGC GGGTCAAGGC GGGTAAGAGG CGGGGTACCG ACTGATTAAA

      2830        2840        2850        2860        2870        2880
TTTTTATTTA TGCAGAGGCC GAGGCCGCCT CGGCCTCTGA GCTATTCCAG AAGTAGTGAG
AAAAATAAAT ACGTCTCCGG CTCCGGCGGA GCCGGAGACT CGATAAGGTC TTCATCACTC

      2890        2900        2910        2920        2930        2940
GAGGCTTTTT TGGAGGCCTA GGCTTTTGCA AAAAGCTTGG ACAGCTCAGG GCTGCGATTT
CTCCGAAAAA ACCTCCGGAT CCGAAAACGT TTTTCGAACC TGTCGAGTCC CGACGCTAAA

      2950        2960        2970        2980        2990        3000
CGCGCCAAAC TTGACGGCAA TCCTAGCGTG AAGGCTGGTA GGATTTTATC CCCGCTGCCA
GCGCGGTTTG AACTGCCGTT AGGATCGCAC TTCCGACCAT CCTAAAATAG GGGCGACGGT
```

FIGURE 19F

pD17-hG1b

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      3010        3020        3030        3040        3050        3060
TCATGGTTCG ACCATTGAAC TGCATCGTCG CCGTGTCCCA AAATATGGGG ATTGGCAAGA
AGTACCAAGC TGGTAACTTG ACGTAGCAGC GGCACAGGGT TTTATACCCC TAACCGTTCT

      3070        3080        3090        3100        3110        3120
ACGGAGACCT ACCCTGGCCT CCGCTCAGGA ACGAGTTCAA GTACTTCCAA AGAATGACCA
TGCCTCTGGA TGGGACCGGA GGCGAGTCCT TGCTCAAGTT CATGAAGGTT TCTTACTGGT

      3130        3140        3150        3160        3170        3180
CAACCTCTTC AGTGGAAGGT AAACAGAATC TGGTGATTAT GGGTAGGAAA ACCTGGTTCT
GTTGGAGAAG TCACCTTCCA TTTGTCTTAG ACCACTAATA CCCATCCTTT TGGACCAAGA

      3190        3200        3210        3220        3230        3240
CCATTCCTGA GAAGAATCGA CCTTTAAAGG ACAGAATTAA TATAGTTCTC AGTAGAGAAC
GGTAAGGACT CTTCTTAGCT GGAAATTTCC TGTCTTAATT ATATCAAGAG TCATCTCTTG

      3250        3260        3270        3280        3290        3300
TCAAAGAACC ACCACGAGGA GCTCATTTTC TTGCCAAAAG TTTGGATGAT GCCTTAAGAC
AGTTTCTTGG TGGTGCTCCT CGAGTAAAAG AACGGTTTTC AAACCTACTA CGGAATTCTG

      3310        3320        3330        3340        3350        3360
TTATTGAACA ACCGGAATTG GCAAGTAAAG TAGACATGGT TTGGATAGTC GGAGGCAGTT
AATAACTTGT TGGCCTTAAC CGTTCATTTC ATCTGTACCA AACCTATCAG CCTCCGTCAA

      3370        3380        3390        3400        3410        3420
CTGTTTACCA GGAAGCCATG AATCAACCAG GCCACCTTAG ACTCTTTGTG ACAAGGATCA
GACAAATGGT CCTTCGGTAC TTAGTTGGTC CGGTGGAATC TGAGAAACAC TGTTCCTAGT

      3430        3440        3450        3460        3470        3480
TGCAGGAATT TGAAAGTGAC ACGTTTTTCC CAGAAATTGA TTTGGGGAAA TATAAACTTC
ACGTCCTTAA ACTTTCACTG TGCAAAAAGG GTCTTTAACT AAACCCCTTT ATATTTGAAG

      3490        3500        3510        3520        3530        3540
TCCCAGAATA CCCAGGCGTC CTCTCTGAGG TCCAGGAGGA AAAAGGCATC AAGTATAAGT
AGGGTCTTAT GGGTCCGCAG GAGAGACTCC AGGTCCTCCT TTTTCCGTAG TTCATATTCA

      3550        3560        3570        3580        3590        3600
TTGAAGTCTA CGAGAAGAAA GACTAACAGG AAGATGCTTT CAAGTTCTCT GCTCCCCTCC
AACTTCAGAT GCTCTTCTTT CTGATTGTCC TTCTACGAAA GTTCAAGAGA CGAGGGGAGG
```

FIGURE 19G

pD17-hG1b

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      3610        3620        3630        3640        3650        3660
TAAAGCTATG CATTTTTATA AGACCATGGG ACTTTTGCTG GCTTTAGATC TCTTTGTGAA
ATTTCGATAC GTAAAAATAT TCTGGTACCC TGAAAACGAC CGAAATCTAG AGAAACACTT

      3670        3680        3690        3700        3710        3720
GGAACCTTAC TTCTGTGGTG TGACATAATT GGACAAACTA CCTACAGAGA TTTAAAGCTC
CCTTGGAATG AAGACACCAC ACTGTATTAA CCTGTTTGAT GGATGTCTCT AAATTTCGAG

      3730        3740        3750        3760        3770        3780
TAAGGTAAAT ATAAAATTTT TAAGTGTATA ATGTGTTAAA CTACTGATTC TAATTGTTTG
ATTCCATTTA TATTTTAAAA ATTCACATAT TACACAATTT GATGACTAAG ATTAACAAAC

      3790        3800        3810        3820        3830        3840
TGTATTTTAG ATTCCAACCT ATGGAACTGA TGAATGGGAG CAGTGGTGGA ATGCCTTTAA
ACATAAAATC TAAGGTTGGA TACCTTGACT ACTTACCCTC GTCACCACCT TACGGAAATT

      3850        3860        3870        3880        3890        3900
TGAGGAAAAC CTGTTTTGCT CAGAAGAAAT GCCATCTAGT GATGATGAGG CTACTGCTGA
ACTCCTTTTG GACAAAACGA GTCTTCTTTA CGGTAGATCA CTACTACTCC GATGACGACT

      3910        3920        3930        3940        3950        3960
CTCTCAACAT TCTACTCCTC CAAAAAAGAA GAGAAAGGTA GAAGACCCCA AGGACTTTCC
GAGAGTTGTA AGATGAGGAG GTTTTTTCTT CTCTTTCCAT CTTCTGGGGT TCCTGAAAGG

      3970        3980        3990        4000        4010        4020
TTCAGAATTG CTAAGTTTTT TGAGTCATGC TGTGTTTAGT AATAGAACTC TTGCTTGCTT
AAGTCTTAAC GATTCAAAAA ACTCAGTACG ACACAAATCA TTATCTTGAG AACGAACGAA

      4030        4040        4050        4060        4070        4080
TGCTATTTAC ACCACAAAGG AAAAAGCTGC ACTGCTATAC AAGAAAATTA TGGAAAAATA
ACGATAAATG TGGTGTTTCC TTTTTCGACG TGACGATATG TTCTTTTAAT ACCTTTTTAT

      4090        4100        4110        4120        4130        4140
TTCTGTAACC TTTATAAGTA GGCATAACAG TTATAATCAT AACATACTGT TTTTTCTTAC
AAGACATTGG AAATATTCAT CCGTATTGTC AATATTAGTA TTGTATGACA AAAAAGAATG

      4150        4160        4170        4180        4190        4200
TCCACACAGG CATAGAGTGT CTGCTATTAA TAACTATGCT CAAAAATTGT GTACCTTTAG
AGGTGTGTCC GTATCTCACA GACGATAATT ATTGATACGA GTTTTTAACA CATGGAAATC
```

FIGURE 19H

pD17-hG1b

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      4210        4220        4230        4240        4250        4260
CTTTTTAATT TGTAAAGGGG TTAATAAGGA ATATTTGATG TATAGTGCCT TGACTAGAGA
GAAAAATTAA ACATTTCCCC AATTATTCCT TATAAACTAC ATATCACGGA ACTGATCTCT

      4270        4280        4290        4300        4310        4320
TCATAATCAG CCATACCACA TTTGTAGAGG TTTTACTTGC TTTAAAAAAC CTCCCACACC
AGTATTAGTC GGTATGGTGT AAACATCTCC AAAATGAACG AAATTTTTTG GAGGGTGTGG

      4330        4340        4350        4360        4370        4380
TCCCCCTGAA CCTGAAACAT AAAATGAATG CAATTGTTGT TGTTAACTTG TTTATTGCAG
AGGGGGACTT GGACTTTGTA TTTTACTTAC GTTAACAACA ACAATTGAAC AAATAACGTC

      4390        4400        4410        4420        4430        4440
CTTATAATGG TTACAAATAA AGCAATAGCA TCACAAATTT CACAAATAAA GCATTTTTTT
GAATATTACC AATGTTTATT TCGTTATCGT AGTGTTTAAA GTGTTTATTT CGTAAAAAAA

      4450        4460        4470        4480        4490        4500
CACTGCATTC TAGTTGTGGT TTGTCCAAAC TCATCAATGT ATCTTATCAT GTCTGGATCG
GTGACGTAAG ATCAACACCA AACAGGTTTG AGTAGTTACA TAGAATAGTA CAGACCTAGC

      4510        4520        4530        4540        4550        4560
GCTGGATGAT CCTCCAGCGC GGGGATCTCA TGCTGGAGTT CTTCGCCCAC CCCAACTTGT
CGACCTACTA GGAGGTCGCG CCCCTAGAGT ACGACCTCAA GAAGCGGGTG GGGTTGAACA

      4570        4580        4590        4600        4610        4620
TTATTGCAGC TTATAATGGT TACAAATAAA GCAATAGCAT CACAAATTTC ACAAATAAAG
AATAACGTCG AATATTACCA ATGTTTATTT CGTTATCGTA GTGTTTAAAG TGTTTATTTC

      4630        4640        4650        4660        4670        4680
CATTTTTTTC ACTGCATTCT AGTTGTGGTT TGTCCAAACT CATCAATGTA TCTTATCATG
GTAAAAAAAG TGACGTAAGA TCAACACCAA ACAGGTTTGA GTAGTTACAT AGAATAGTAC

      4690        4700        4710        4720        4730        4740
TCTGTATACC GTCGACCTCT AGCTAGAGCT TGGCGTAATC ATGGTCATAG CTGTTTCCTG
AGACATATGG CAGCTGGAGA TCGATCTCGA ACCGCATTAG TACCAGTATC GACAAAGGAC

      4750        4760        4770        4780        4790        4800
TGTGAAATTG TTATCCGCTC ACAATTCCAC ACAACATACG AGCCGGAAGC ATAAAGTGTA
ACACTTTAAC AATAGGCGAG TGTTAAGGTG TGTTGTATGC TCGGCCTTCG TATTTCACAT
```

FIGURE 19I

pD17-hG1b

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        4810        4820        4830        4840        4850        4860
AAGCCTGGGG TGCCTAATGA GTGAGCTAAC TCACATTAAT TGCGTTGCGC TCACTGCCCG
TTCGGACCCC ACGGATTACT CACTCGATTG AGTGTAATTA ACGCAACGCG AGTGACGGGC

        4870        4880        4890        4900        4910        4920
CTTTCCAGTC GGGAAACCTG TCGTGCCAGC TGCATTAATG AATCGGCCAA CGCGCGGGGA
GAAAGGTCAG CCCTTTGGAC AGCACGGTCG ACGTAATTAC TTAGCCGGTT GCGCGCCCCT

        4930        4940        4950        4960        4970        4980
GAGGCGGTTT GCGTATTGGG CGCTCTTCCG CTTCCTCGCT CACTGACTCG CTGCGCTCGG
CTCCGCCAAA CGCATAACCC GCGAGAAGGC GAAGGAGCGA GTGACTGAGC GACGCGAGCC

        4990        5000        5010        5020        5030        5040
TCGTTCGGCT GCGGCGAGCG GTATCAGCTC ACTCAAAGGC GGTAATACGG TTATCCACAG
AGCAAGCCGA CGCCGCTCGC CATAGTCGAG TGAGTTTCCG CCATTATGCC AATAGGTGTC

        5050        5060        5070        5080        5090        5100
AATCAGGGGA TAACGCAGGA AAGAACATGT GAGCAAAAGG CCAGCAAAAG GCCAGGAACC
TTAGTCCCCT ATTGCGTCCT TTCTTGTACA CTCGTTTTCC GGTCGTTTTC CGGTCCTTGG

        5110        5120        5130        5140        5150        5160
GTAAAAAGGC CGCGTTGCTG GCGTTTTTCC ATAGGCTCCG CCCCCCTGAC GAGCATCACA
CATTTTTCCG GCGCAACGAC CGCAAAAAGG TATCCGAGGC GGGGGGACTG CTCGTAGTGT

        5170        5180        5190        5200        5210        5220
AAAATCGACG CTCAAGTCAG AGGTGGCGAA ACCCGACAGG ACTATAAAGA TACCAGGCGT
TTTTAGCTGC GAGTTCAGTC TCCACCGCTT TGGGCTGTCC TGATATTTCT ATGGTCCGCA

        5230        5240        5250        5260        5270        5280
TTCCCCCTGG AAGCTCCCTC GTGCGCTCTC CTGTTCCGAC CCTGCCGCTT ACCGGATACC
AAGGGGGACC TTCGAGGGAG CACGCGAGAG GACAAGGCTG GGACGGCGAA TGGCCTATGG

        5290        5300        5310        5320        5330        5340
TGTCCGCCTT TCTCCCTTCG GGAAGCGTGG CGCTTTCTCA ATGCTCACGC TGTAGGTATC
ACAGGCGGAA AGAGGGAAGC CCTTCGCACC GCGAAAGAGT TACGAGTGCG ACATCCATAG

        5350        5360        5370        5380        5390        5400
TCAGTTCGGT GTAGGTCGTT CGCTCCAAGC TGGGCTGTGT GCACGAACCC CCCGTTCAGC
AGTCAAGCCA CATCCAGCAA GCGAGGTTCG ACCCGACACA CGTGCTTGGG GGGCAAGTCG
```

FIGURE 19J

pD17-hG1b

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      5410        5420        5430        5440        5450        5460
CCGACCGCTG CGCCTTATCC GGTAACTATC GTCTTGAGTC CAACCCGGTA AGACACGACT
GGCTGGCGAC GCGGAATAGG CCATTGATAG CAGAACTCAG GTTGGGCCAT TCTGTGCTGA

      5470        5480        5490        5500        5510        5520
TATCGCCACT GGCAGCAGCC ACTGGTAACA GGATTAGCAG AGCGAGGTAT GTAGGCGGTG
ATAGCGGTGA CCGTCGTCGG TGACCATTGT CCTAATCGTC TCGCTCCATA CATCCGCCAC

      5530        5540        5550        5560        5570        5580
CTACAGAGTT CTTGAAGTGG TGGCCTAACT ACGGCTACAC TAGAAGGACA GTATTTGGTA
GATGTCTCAA GAACTTCACC ACCGGATTGA TGCCGATGTG ATCTTCCTGT CATAAACCAT

      5590        5600        5610        5620        5630        5640
TCTGCGCTCT GCTGAAGCCA GTTACCTTCG GAAAAAGAGT TGGTAGCTCT TGATCCGGCA
AGACGCGAGA CGACTTCGGT CAATGGAAGC CTTTTTCTCA ACCATCGAGA ACTAGGCCGT

      5650        5660        5670        5680        5690        5700
AACAAACCAC CGCTGGTAGC GGTGGTTTTT TTGTTTGCAA GCAGCAGATT ACGCGCAGAA
TTGTTTGGTG GCGACCATCG CCACCAAAAA AACAAACGTT CGTCGTCTAA TGCGCGTCTT

      5710        5720        5730        5740        5750        5760
AAAAAGGATC TCAAGAAGAT CCTTTGATCT TTTCTACGGG GTCTGACGCT CAGTGGAACG
TTTTTCCTAG AGTTCTTCTA GGAAACTAGA AAAGATGCCC CAGACTGCGA GTCACCTTGC

      5770        5780        5790        5800        5810        5820
AAAACTCACG TTAAGGGATT TTGGTCATGA GATTATCAAA AAGGATCTTC ACCTAGATCC
TTTTGAGTGC AATTCCCTAA AACCAGTACT CTAATAGTTT TTCCTAGAAG TGGATCTAGG

      5830        5840        5850        5860        5870        5880
TTTTAAATTA AAAATGAAGT TTTAAATCAA TCTAAAGTAT ATATGAGTAA ACTTGGTCTG
AAAATTTAAT TTTTACTTCA AAATTTAGTT AGATTTCATA TATACTCATT TGAACCAGAC

      5890        5900        5910        5920        5930        5940
ACAGTTACCA ATGCTTAATC AGTGAGGCAC CTATCTCAGC GATCTGTCTA TTTCGTTCAT
TGTCAATGGT TACGAATTAG TCACTCCGTG GATAGAGTCG CTAGACAGAT AAAGCAAGTA

      5950        5960        5970        5980        5990        6000
CCATAGTTGC CTGACTCCCC GTCGTGTAGA TAACTACGAT ACGGGAGGGC TTACCATCTG
GGTATCAACG GACTGAGGGG CAGCACATCT ATTGATGCTA TGCCCTCCCG AATGGTAGAC
```

FIGURE 19K

pD17-hG1b

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      6010        6020        6030        6040        6050        6060
GCCCCAGTGC TGCAATGATA CCGCGAGACC CACGCTCACC GGCTCCAGAT TTATCAGCAA
CGGGGTCACG ACGTTACTAT GGCGCTCTGG GTGCGAGTGG CCGAGGTCTA AATAGTCGTT

      6070        6080        6090        6100        6110        6120
TAAACCAGCC AGCCGGAAGG GCCGAGCGCA GAAGTGGTCC TGCAACTTTA TCCGCCTCCA
ATTTGGTCGG TCGGCCTTCC CGGCTCGCGT CTTCACCAGG ACGTTGAAAT AGGCGGAGGT

      6130        6140        6150        6160        6170        6180
TCCAGTCTAT TAATTGTTGC CGGGAAGCTA GAGTAAGTAG TTCGCCAGTT AATAGTTTGC
AGGTCAGATA ATTAACAACG GCCCTTCGAT CTCATTCATC AAGCGGTCAA TTATCAAACG

      6190        6200        6210        6220        6230        6240
GCAACGTTGT TGCCATTGCT ACAGGCATCG TGGTGTCACG CTCGTCGTTT GGTATGGCTT
CGTTGCAACA ACGGTAACGA TGTCCGTAGC ACCACAGTGC GAGCAGCAAA CCATACCGAA

      6250        6260        6270        6280        6290        6300
CATTCAGCTC CGGTTCCCAA CGATCAAGGC GAGTTACATG ATCCCCCATG TTGTGCAAAA
GTAAGTCGAG GCCAAGGGTT GCTAGTTCCG CTCAATGTAC TAGGGGGTAC AACACGTTTT

      6310        6320        6330        6340        6350        6360
AAGCGGTTAG CTCCTTCGGT CCTCCGATCG TTGTCAGAAG TAAGTTGGCC GCAGTGTTAT
TTCGCCAATC GAGGAAGCCA GGAGGCTAGC AACAGTCTTC ATTCAACCGG CGTCACAATA

      6370        6380        6390        6400        6410        6420
CACTCATGGT TATGGCAGCA CTGCATAATT CTCTTACTGT CATGCCATCC GTAAGATGCT
GTGAGTACCA ATACCGTCGT GACGTATTAA GAGAATGACA GTACGGTAGG CATTCTACGA

      6430        6440        6450        6460        6470        6480
TTTCTGTGAC TGGTGAGTAC TCAACCAAGT CATTCTGAGA ATAGTGTATG CGGCGACCGA
AAAGACACTG ACCACTCATG AGTTGGTTCA GTAAGACTCT TATCACATAC GCCGCTGGCT

      6490        6500        6510        6520        6530        6540
GTTGCTCTTG CCCGGCGTCA ATACGGGATA ATACCGCGCC ACATAGCAGA ACTTTAAAAG
CAACGAGAAC GGGCCGCAGT TATGCCCTAT TATGGCGCGG TGTATCGTCT TGAAATTTTC

      6550        6560        6570        6580        6590        6600
TGCTCATCAT TGGAAAACGT TCTTCGGGGC GAAAACTCTC AAGGATCTTA CCGCTGTTGA
ACGAGTAGTA ACCTTTTGCA AGAAGCCCCG CTTTTGAGAG TTCCTAGAAT GGCGACAACT
```

FIGURE 19L

pD17-hG1b

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      6610        6620        6630        6640        6650        6660
GATCCAGTTC GATGTAACCC ACTCGTGCAC CCAACTGATC TTCAGCATCT TTTACTTTCA
CTAGGTCAAG CTACATTGGG TGAGCACGTG GGTTGACTAG AAGTCGTAGA AAATGAAAGT

      6670        6680        6690        6700        6710        6720
CCAGCGTTTC TGGGTGAGCA AAAACAGGAA GGCAAAATGC CGCAAAAAAG GGAATAAGGG
GGTCGCAAAG ACCCACTCGT TTTTGTCCTT CCGTTTTACG GCGTTTTTTC CCTTATTCCC

      6730        6740        6750        6760        6770        6780
CGACACGGAA ATGTTGAATA CTCATACTCT TCCTTTTTCA ATATTATTGA AGCATTTATC
GCTGTGCCTT TACAACTTAT GAGTATGAGA AGGAAAAAGT TATAATAACT TCGTAAATAG

      6790        6800        6810        6820        6830        6840
AGGGTTATTG TCTCATGAGC GGATACATAT TTGAATGTAT TTAGAAAAAT AAACAAATAG
TCCCAATAAC AGAGTACTCG CCTATGTATA AACTTACATA AATCTTTTTA TTTGTTTATC

      6850        6860        6870        6880        6890        6900
GGGTTCCGCG CACATTTCCC CGAAAAGTGC CACCTGACGT CGACGGATCG GGAGATCTGC
CCCAAGGCGC GTGTAAAGGG GCTTTTCACG GTGGACTGCA GCTGCCTAGC CCTCTAGACG

      6910        6920        6930        6940        6950        6960
TAGGTGACCT GAGGCGCGCC GGCTTCGAAT AGCCAGAGTA ACCTTTTTTT TTAATTTTAT
ATCCACTGGA CTCCGCGCGG CCGAAGCTTA TCGGTCTCAT TGGAAAAAAA AATTAAAATA

      6970        6980        6990        7000        7010        7020
TTTATTTTAT TTTTGAGATG GAGTTTGGCG CCGATCTCCC GATCCCCTAT GGTCGACTCT
AAATAAAATA AAAACTCTAC CTCAAACCGC GGCTAGAGGG CTAGGGGATA CCAGCTGAGA

      7030        7040        7050        7060        7070        7080
CAGTACAATC TGCTCTGATG CCGCATAGTT AAGCCAGTAT CTGCTCCCTG CTTGTGTGTT
GTCATGTTAG ACGAGACTAC GGCGTATCAA TTCGGTCATA GACGAGGGAC GAACACACAA

      7090        7100        7110        7120        7130        7140
GGAGGTCGCT GAGTAGTGCG CGAGCAAAAT TTAAGCTACA ACAAGGCAAG GCTTGACCGA
CCTCCAGCGA CTCATCACGC GCTCGTTTTA AATTCGATGT TGTTCCGTTC CGAACTGGCT

      7150        7160        7170        7180        7190        7200
CAATTGCATG AAGAATCTGC TTAGGGTTAG GCGTTTTGCG CTGCTTCGCG ATGTACGGGC
GTTAACGTAC TTCTTAGACG AATCCCAATC CGCAAAACGC GACGAAGCGC TACATGCCCG
```

FIGURE 19M

pD17-hG1b

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      7210        7220        7230        7240        7250        7260
CAGATATACG CGTTGACATT GATTATTGAC TAGTTATTAA TAGTAATCAA TTACGGGGTC
GTCTATATGC GCAACTGTAA CTAATAACTG ATCAATAATT ATCATTAGTT AATGCCCCAG

      7270        7280        7290        7300        7310        7320
ATTAGTTCAT AGCCCATATA TGGAGTTCCG CGTTACATAA CTTACGGTAA ATGGCCCGCC
TAATCAAGTA TCGGGTATAT ACCTCAAGGC GCAATGTATT GAATGCCATT TACCGGGCGG

      7330        7340        7350        7360        7370        7380
TGGCTGACCG CCCAACGACC CCCGCCCATT GACGTCAATA ATGACGTATG TTCCCATAGT
ACCGACTGGC GGGTTGCTGG GGGCGGGTAA CTGCAGTTAT TACTGCATAC AAGGGTATCA

      7390        7400        7410        7420        7430        7440
AACGCCAATA GGGACTTTCC ATTGACGTCA ATGGGTGGAC TATTTACGGT AAACTGCCCA
TTGCGGTTAT CCCTGAAAGG TAACTGCAGT TACCCACCTG ATAAATGCCA TTTGACGGGT

      7450        7460        7470        7480        7490        7500
CTTGGCAGTA CATCAAGTGT ATCATATGCC AAGTACGCCC CCTATTGACG TCAATGACGG
GAACCGTCAT GTAGTTCACA TAGTATACGG TTCATGCGGG GGATAACTGC AGTTACTGCC

      7510        7520        7530        7540        7550        7560
TAAATGGCCC GCCTGGCATT ATGCCCAGTA CATGACCTTA TGGGACTTTC CTACTTGGCA
ATTTACCGGG CGGACCGTAA TACGGGTCAT GTACTGGAAT ACCCTGAAAG GATGAACCGT

      7570        7580        7590        7600        7610        7620
GTACATCTAC GTATTAGTCA TCGCTATTAC CATGGTGATG CGGTTTTGGC AGTACATCAA
CATGTAGATG CATAATCAGT AGCGATAATG GTACCACTAC GCCAAAACCG TCATGTAGTT

      7630        7640        7650        7660        7670        7680
TGGGCGTGGA TAGCGGTTTG ACTCACGGGG ATTTCCAAGT CTCCACCCCA TTGACGTCAA
ACCCGCACCT ATCGCCAAAC TGAGTGCCCC TAAAGGTTCA GAGGTGGGGT AACTGCAGTT

      7690        7700        7710        7720        7730        7740
TGGGAGTTTG TTTTGGCACC AAAATCAACG GGACTTTCCA AAATGTCGTA ACAACTCCGC
ACCCTCAAAC AAAACCGTGG TTTTAGTTGC CCTGAAAGGT TTTACAGCAT TGTTGAGGCG

      7750        7760        7770        7780        7790        7800
CCCATTGACG CAAATGGGCG GTAGGCGTGT ACGGTGGGAG GTCTATATAA GCAGAGCTCT
GGGTAACTGC GTTTACCCGC CATCCGCACA TGCCACCCTC CAGATATATT CGTCTCGAGA
```

FIGURE 19N

pD17-hG1b

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      7810        7820        7830        7840        7850        7860
CTGGCTAACT AGAGAACCCA CTGCTTACTG GCTTATCGAA ATTAATACGA CTCACTATAG
GACCGATTGA TCTCTTGGGT GACGAATGAC CGAATAGCTT TAATTATGCT GAGTGATATC

      7870        7880
GGAGACCCAA GCTT
CCTCTGGGTT CGAA
```

FIGURE 20

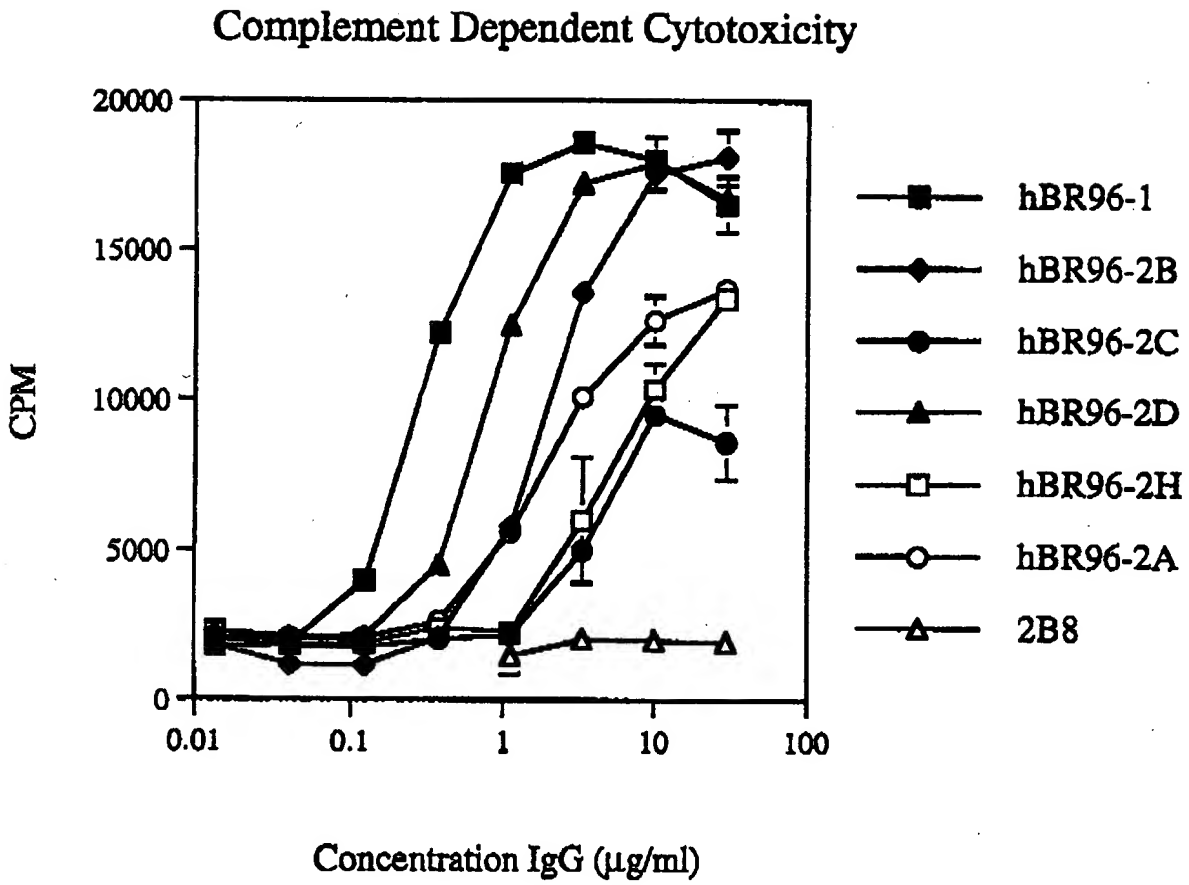
Complement Dependent Cytotoxicity
CPM
20000
15000
10000
5000
0
0.01
0.1
1
10
100
Concentration IgG (µg/ml)
hBR96-1
hBR96-2B
hBR96-2C
hBR96-2D
hBR96-2H
hBR96-2A
2B8

FIGURE 21

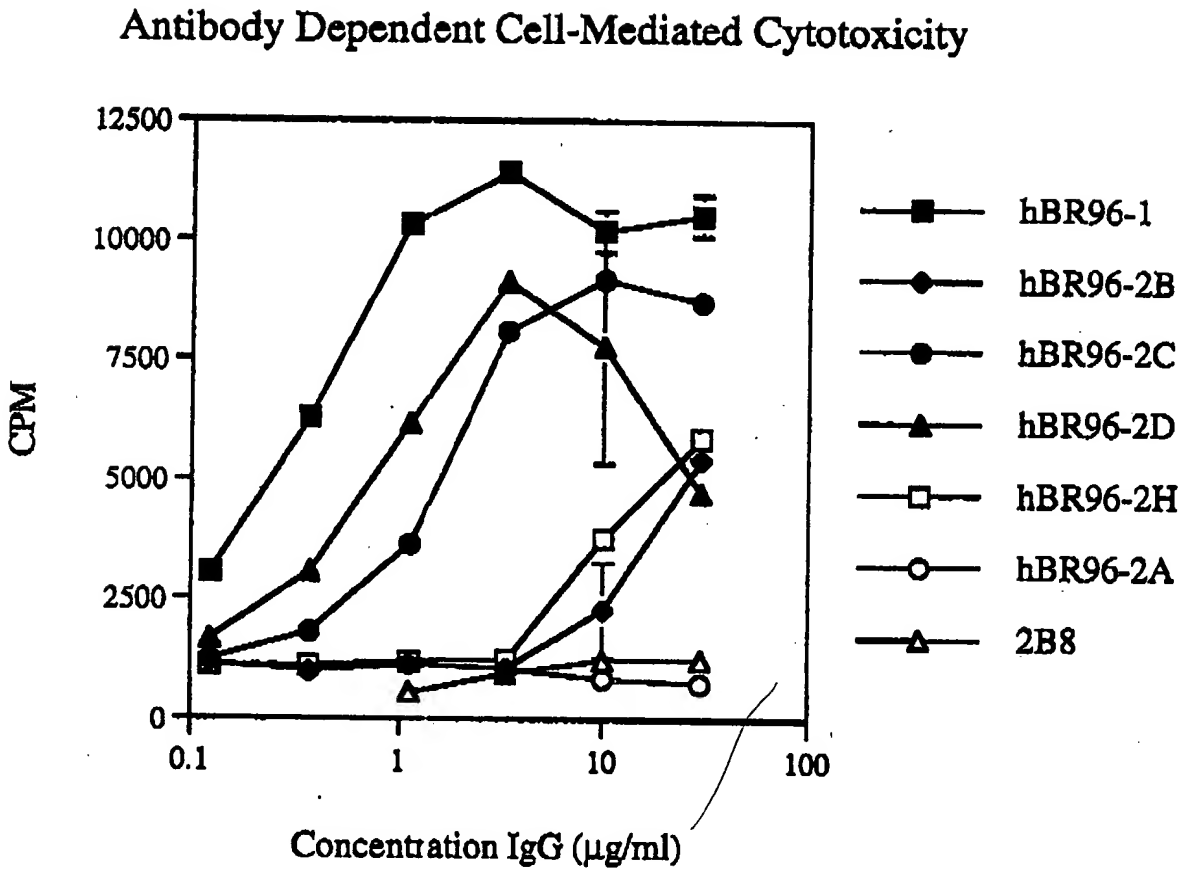
Antibody Dependent Cell-Mediated Cytotoxicity
CPM
12500
10000
7500
5000
2500
0
0.1
1
10
100
Concentration IgG (µg/ml)
hBR96-1
hBR96-2B
hBR96-2C
hBR96-2D
hBR96-2H
hBR96-2A
2B8

FIGURE 22

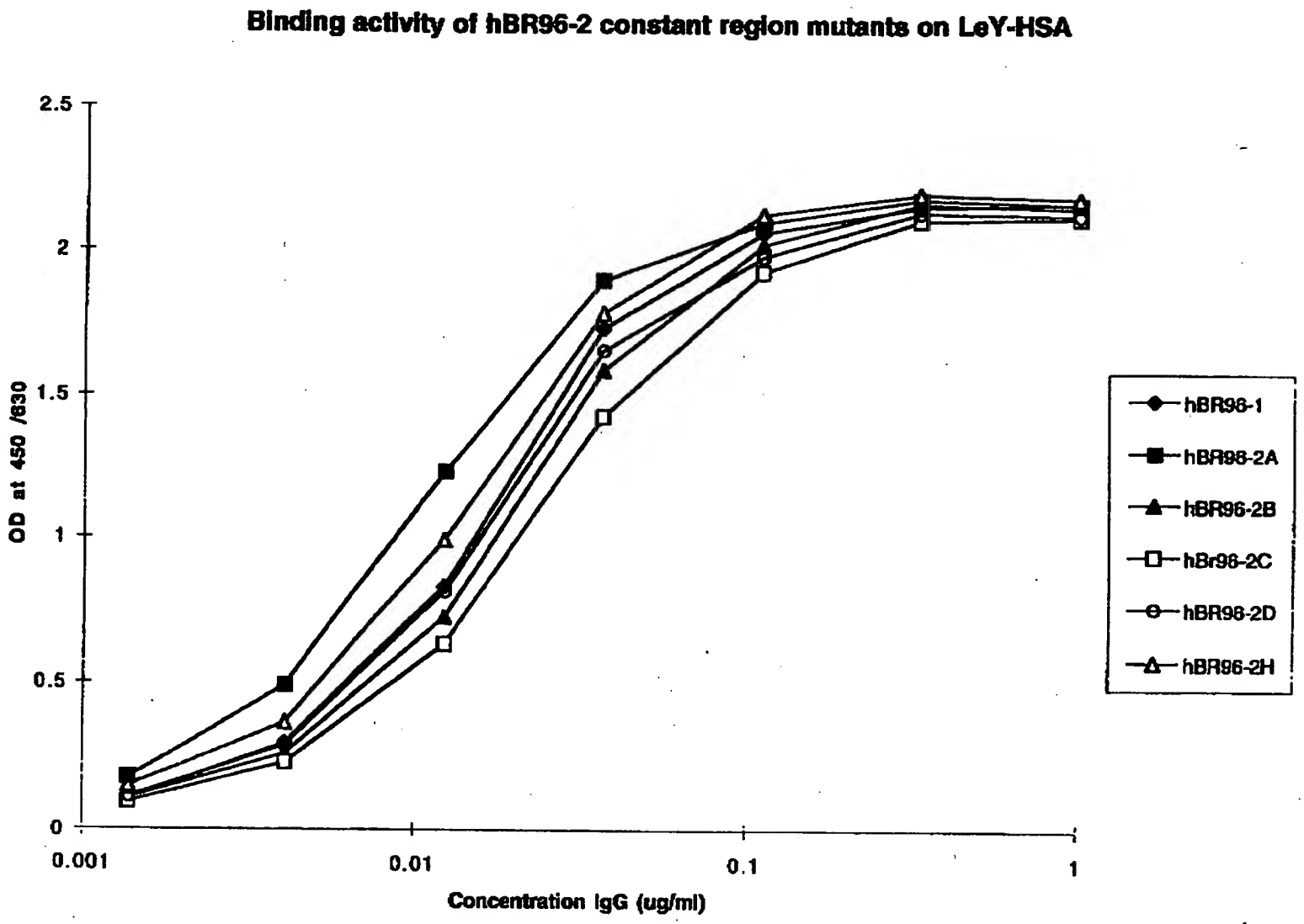
Binding activity of hBR96-2 constant region mutants on LeY-HSA
OD at 450 /630
2.5
2
1.5
1
0.5
0
0.001
0.01
0.1
1
Concentration IgG (ug/ml)
hBR96-1
hBR96-2A
hBR96-2B
hBr96-2C
hBR96-2D
hBR96-2H

FIGURE 23

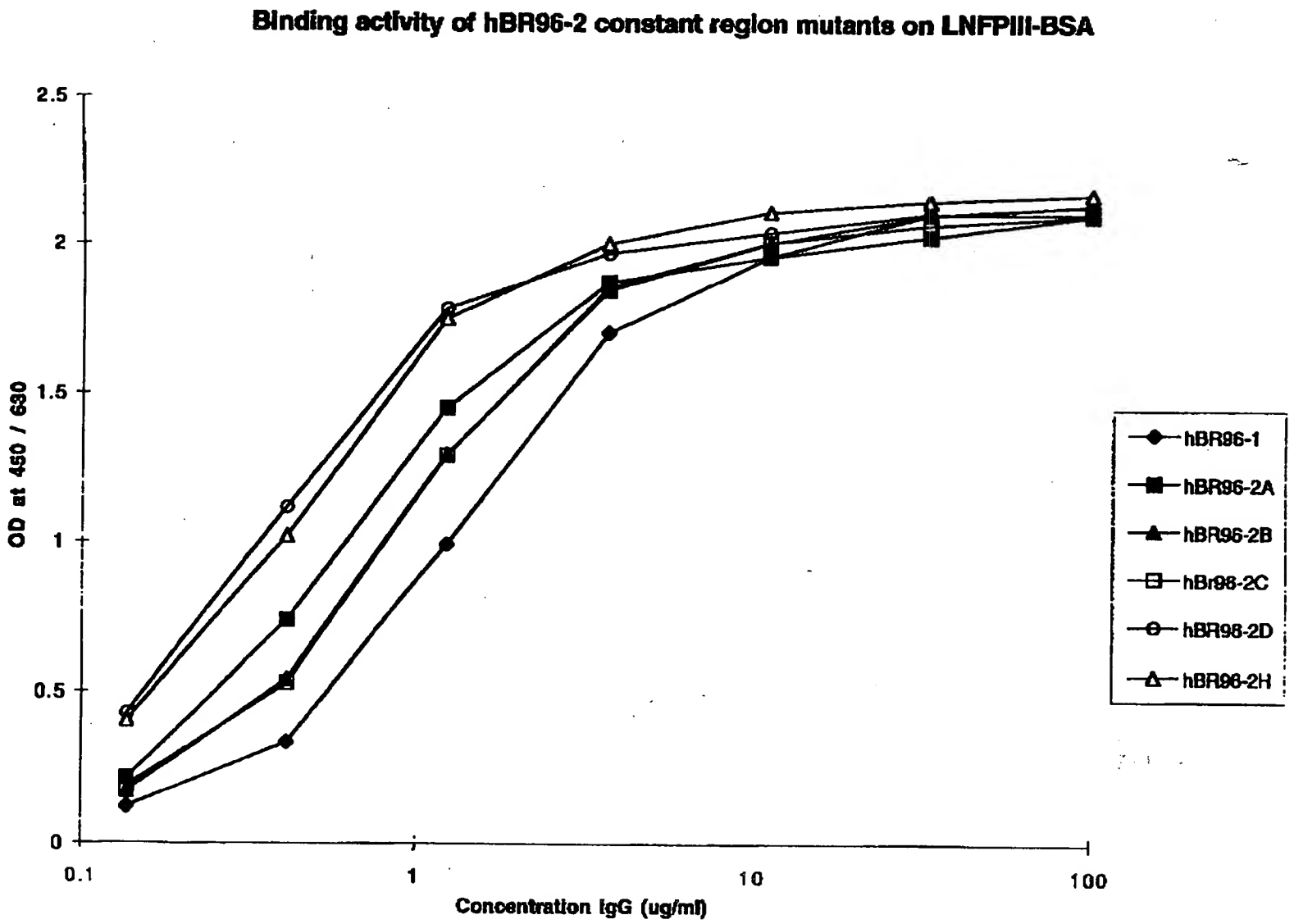
Binding activity of hBR96-2 constant region mutants on LNFPIII-BSA
OD at 450 / 630
2.5
2
1.5
1
0.5
0
0.1
1
10
100
Concentration IgG (ug/ml)
hBR96-1
hBR96-2A
hBR96-2B
hBr96-2C
hBR96-2D
hBR96-2H

Figure 24

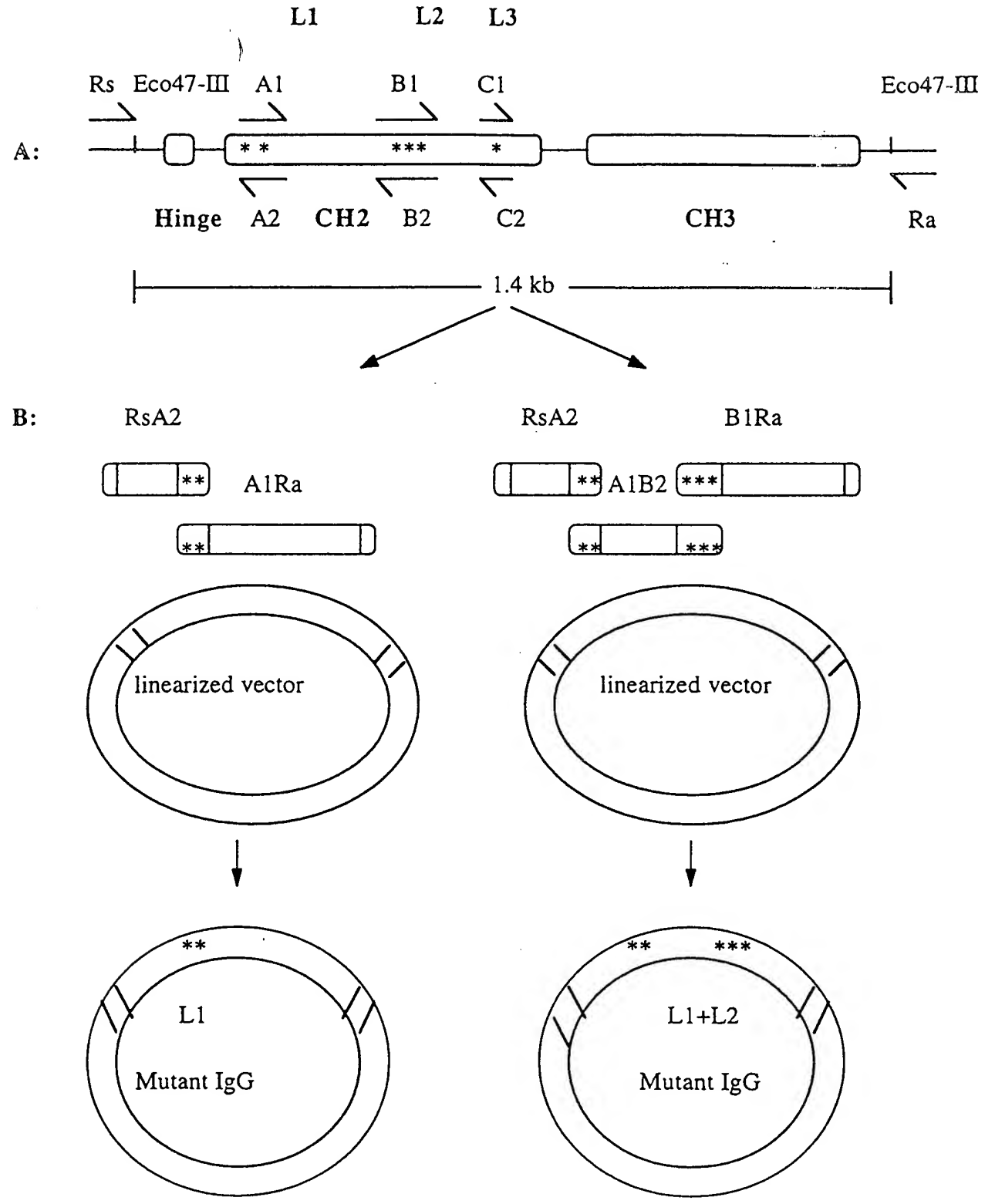

Figure 25

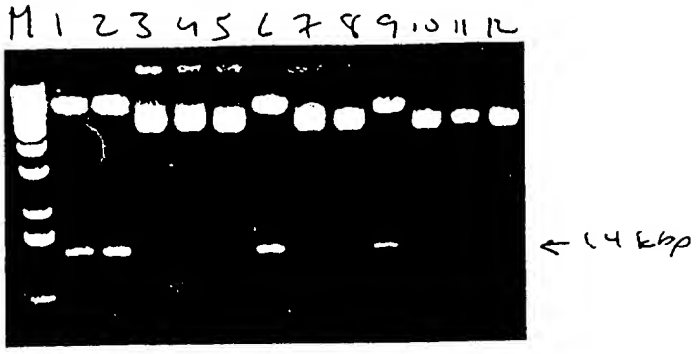

Figure 26

hBR96-2 Heavy Chain Variable Region (V_H)

```
1          11         21         31         41
EVQLVESGGG LVQPGGSLRL SCAASGFPFS DYYMYWVRQA PGKGLEWVSY
51         61         71         81         91
ISQDGDITDY ADSVKGRFTI SRDNAKNSLY LQMNSLRDED TAVYYCARGL
101        111
ADGAWFAYWG QGTLVTVSS
```

human IgG1 constant

```
                                 |CH1
                                 A STKGPSVFPL APSSKSTSGG TAALGCLVKD
YFPEPVTVSW NSGALTSGVH TFPAVLQSSG LYSLSSVVTV PSSSLGTQTY
                                 |CH2 235 237
ICNVNHKPSN TKVDKKVEPK SCDKTHTCPP CPAPELLGGP SVFLFPPKPK
DTLMISRTPE VTCVVVDVSH EDPEVKFNWY VDGVEVHNAK TKPREEQYNS
                     318 320 322 331        |CH3
TYRVVSVLTV LHQDWLNGKE YKCKVSNKAL PAPIEKTISK AKGQPREPQV
YTLPPSRDEL TKNQVSLTCL VKGFYPSDIA VEWESNGQPE NNYKTTPPVL
DSDGSFFLYS KLTVDKSRWQ QGNVFSCSVM HEALHNHYTQ KSLSLSPGK
```

Figure 27

hBR96-2A: Heavy Chain Variable Region (V_H)

```
1          11         21         31         41
EVQLVESGGG LVQPGGSLRL SCAASGFPFS DYYMYWVRQA PGKGLEWVSY

51         61         71         81         91
ISQDGDITDY ADSVKGRFTI SRDNAKNSLY LQMNSLRDED TAVYYCARGL

101        111
ADGAWFAYWG QGTLVTVSS
```

hBR96-2A: Human Heavy Chain IgG1 Constant Region ΔCH2

```
A STKGPSVFPL APSSKSTSGG TAALGCLVKD YFPEPVTVSW NSGALTSGVH

TFPAVLQSSG LYSLSSVVTV PSSSLGTQTY ICNVNHKPSN TKVDKKVEPK

SCDKTHTCPP CP    GQPREPQV YTLPPSRDEL TKNQVSLTCL VKGFYPSDIA

VEWESNGQPE NNYKTTPPVL DSDGSFFLYS KLTVDKSRWQ QGNVFSCSVM

HEALHNHYTQ KSLSLSPGK
```

Figure 28

This sequence is the chi BR96 IgG1 with CH2 deleted.

VH

```
  1  EVNLVESGGG LVQPGGSLKV SCVTSGFTFS DYYMYWVRQT PEKRLEWVAY
 51  ISQGGDITDY PDTVKGRFTI SRDNAKNTLY LQMSRLKSED TAMYYCARGL
101  DDGAWFAYWG QGTLVTVSVA STKGPSVFPL APSSKSTSGG TAALGCLVKD
151  YFPEPVTVSW NSGALTSGVH TFPAVLQSSG LYSLSSVVTV PSSSLGTQTY
201  ICNVNHKPSN TKVDKKVEPK SCDKTHTCPP CPGQPREPQV YTLPPSRDEL
251  TKNQVSLTCL VKGFYPSDIA VEWESNGQPE NNYKTTPPVL DSDGSFFLYS
301  KLTVDKSRWQ QGNVFSCSVM HEALHNHYTQ KSLSLSPGK
```

CH1

CH3